```
=> s l1 and review
L4        1152 L1 AND REVIEW

=> dis his

     (FILE 'HOME' ENTERED AT 12:25:10 ON 21 FEB 2003)

     FILE 'MEDLINE, SCISEARCH, LIFESCI, BIOTECHDS, BIOSIS, EMBASE, HCAPLUS,
     NTIS, ESBIOBASE, BIOTECHNO, WPIDS' ENTERED AT 12:25:17 ON 21 FEB 2003
L1         29774 S RAF
L2            37 S L1 (10A) ANGIOGENE?
L3            10 DUP REM L2 (27 DUPLICATES REMOVED)
L4          1152 S L1 AND REVIEW

=> log h
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                                                         ENTRY    SESSION
FULL ESTIMATED COST                                      35.51      35.72

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
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NEWS 2	Apr 08	"Ask CAS" for self-help around the clock
NEWS 3	Apr 09	BEILSTEIN: Reload and Implementation of a New Subject Area
NEWS 4	Apr 09	ZDB will be removed from STN
NEWS 5	Apr 19	US Patent Applications available in IFICDB, IFIPAT, and IFIUDB
NEWS 6	Apr 22	Records from IP.com available in CAPLUS, HCAPLUS, and ZCAPLUS
NEWS 7	Apr 22	BIOSIS Gene Names now available in TOXCENTER
NEWS 8	Apr 22	Federal Research in Progress (FEDRIP) now available
NEWS 9	Jun 03	New e-mail delivery for search results now available
NEWS 10	Jun 10	MEDLINE Reload
NEWS 11	Jun 10	PCTFULL has been reloaded
NEWS 12	Jul 02	FOREGE no longer contains STANDARDS file segment
NEWS 13	Jul 22	USAN to be reloaded July 28, 2002; saved answer sets no longer valid
NEWS 14	Jul 29	Enhanced polymer searching in REGISTRY
NEWS 15	Jul 30	NETFIRST to be removed from STN
NEWS 16	Aug 08	CANCERLIT reload
NEWS 17	Aug 08	PHARMAMarketLetter(PHARMAML) - new on STN
NEWS 18	Aug 08	NTIS has been reloaded and enhanced
NEWS 19	Aug 19	Aquatic Toxicity Information Retrieval (AQUIRE) now available on STN
NEWS 20	Aug 19	IFIPAT, IFICDB, and IFIUDB have been reloaded
NEWS 21	Aug 19	The MEDLINE file segment of TOXCENTER has been reloaded
NEWS 22	Aug 26	Sequence searching in REGISTRY enhanced
NEWS 23	Sep 03	JAPIO has been reloaded and enhanced
NEWS 24	Sep 16	Experimental properties added to the REGISTRY file
NEWS 25	Sep 16	CA Section Thesaurus available in CAPLUS and CA
NEWS 26	Oct 01	CASREACT Enriched with Reactions from 1907 to 1985
NEWS 27	Oct 21	EVENTLINE has been reloaded
NEWS 28	Oct 24	BEILSTEIN adds new search fields
NEWS 29	Oct 24	Nutraceuticals International (NUTRACEUT) now available on STN
NEWS 30	Oct 25	MEDLINE SDI run of October 8, 2002
NEWS 31	Nov 18	DKILIT has been renamed APOLLIT
NEWS 32	Nov 25	More calculated properties added to REGISTRY
NEWS 33	Dec 02	TIBKAT will be removed from STN
NEWS 34	Dec 04	CSA files on STN
NEWS 35	Dec 17	PCTFULL now covers WP/PCT Applications from 1978 to date
NEWS 36	Dec 17	TOXCENTER enhanced with additional content
NEWS 37	Dec 17	Adis Clinical Trials Insight now available on STN
NEWS 38	Dec 30	ISMEC no longer available
NEWS 39	Jan 13	Indexing added to some pre-1967 records in CA/CAPLUS
NEWS 40	Jan 21	NUTRACEUT offering one free connect hour in February 2003
NEWS 41	Jan 21	PHARMAML offering one free connect hour in February 2003
NEWS 42	Jan 29	Simultaneous left and right truncation added to COMPENDEX, ENERGY, INSPEC
NEWS 43	Feb 13	CANCERLIT is no longer being updated

NEWS EXPRESS	January 6 CURRENT WINDOWS VERSION IS V6.01a, CURRENT MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP), AND CURRENT DISCOVER FILE IS DATED 01 OCTOBER 2002
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NEWS INTER	General Internet Information
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 NEWS WWW      CAS World Wide Web Site (general information)

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                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.21       0.21

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=> s raf-caax
L1           84 RAF-CAAX

=> s l1 and angiogene?
L2            3 L1 AND ANGIOGENE?

=> dup rem l2
PROCESSING COMPLETED FOR L2
L3            2 DUP REM L2 (1 DUPLICATE REMOVED)

=> d 1,2
```

L3 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2003 ACS DUPLICATE 1
AN 2001:137041 HCAPLUS
DN 134:188193
TI Protein and cDNA sequences of modified human protein kinase C-Raf and/or H-Ras and therapeutic uses thereof for modulation of **angiogenesis**
IN Hood, John; Eliceiri, Brian; Cheresh, David A.
PA The Scripps Research Institute, USA
SO PCT Int. Appl., 102 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001012210	A1	20010222	WO 2000-US21842	20000811
	WO 2001012210	C2	20020912		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1210099	A1	20020605	EP 2000-955423	20000811
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
	NO 2002000718	A	20020410	NO 2002-718	20020212
PRAI	US 1999-148924P	P	19990813		
	US 2000-215951P	P	20000705		
	WO 2000-US21842	W	20000811		

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 2 Elsevier BIOBASE COPYRIGHT 2003 Elsevier Science B.V.
AN 1998104625 ESBIOBASE
TI Activation of tissue-factor gene expression in breast carcinoma cells by stimulation of the RAF-ERK signaling pathway
AU Zhou J.-N.; Ljungdahl S.; Shoshan M.C.; Swedenborg J.; Linder S.
CS S. Linder, Radiumhemmets Research Laboratory, Department of Oncology-Pathology, Karolinska Institute and Hospital, S-171 76 Stockholm, Sweden.
SO Molecular Carcinogenesis, (1998), 21/4 (234-243), 25 reference(s)
CODEN: MOCAE8 ISSN: 0899-1987
DT Journal; Article
CY United States
LA English
SL English

=> d 2 ab

L3 ANSWER 2 OF 2 Elsevier BIOBASE COPYRIGHT 2003 Elsevier Science B.V.
AB Tissue factor (TF) is a cell-surface glycoprotein responsible for initiating the extrinsic pathway of coagulation. The overexpression of TF in human malignancy has been correlated with the angiogenic phenotype, poor prognosis, and thromboembolic complications. The mechanisms underlying constitutive expression of TF in cancer cells are poorly defined. We cloned TF cDNA on the basis of its strong expression in metastatic MDA-MB-231 breast carcinoma cells in contrast to its weak expression in non-metastatic MCF-7 cells. Transient transfection analysis showed that TF promoter activity in MCF-7 cells could be stimulated by expression of a membrane-targeted raf kinase (**raf-CAAX**
). raf-induced activity was dependent on the presence of an AP-1/NF.kappa.B motif in the TF promoter and was inhibited by dominant-negative mutants of jun and by I-kB.alpha.. MDA-MB-231 cells were found to contain higher levels of ERK1/2 kinase activity than did

MCF-7 cells. Electrophoret[redacted] mobility shift assays showed t[redacted] MDA-MB-231 nuclear proteins bound strongly to an oligonucleotide corresponding to the AP-1/NF-.kappa.B sequence, whereas MCF- 7 nuclear extracts showed weak binding to this element. Finally, we showed that TF mRNA levels in MDA-MB-231 cells declined after addition of the mitogen-activated protein kinase kinase inhibitor PD98059. Our data showed that activation of the raf-ERK pathway led to activation of TF expression in breast carcinoma cells and suggested that constitutive activation of this pathway leads to high TF expression in MDA-MB-231 cells.

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=> d 2 kwic

L3    ANSWER 2 OF 2  Elsevier BIOBASE  COPYRIGHT 2003 Elsevier Science B.V.
AB.   . . transfection analysis showed that TF promoter activity in MCF-7
      cells could be stimulated by expression of a membrane-targeted raf kinase
      (raf-CAAX). raf-induced activity was dependent on the
      presence of an AP-1/NF.kappa.B motif in the TF promoter and was inhibited
      by dominant-negative. . .
CC.   . . Growth Control: Growth factors and inhibitors
      87.3.2.3 CANCER RESEARCH: DIAGNOSIS AND PROGNOSIS: Molecular and Cellular
      Techniques: Histopathology
      87.2.6 CANCER RESEARCH: TUMOUR BIOLOGY: Angiogenesis and the
      Tumour Vascular System
      87.5.11 CANCER RESEARCH: CLINICAL INVESTIGATIONS BY ORGAN SITE: Breast


=> s l1 and py<1990
   3 FILES SEARCHED...
   5 FILES SEARCHED...
   8 FILES SEARCHED...
L4            0 L1 AND PY<1990

=> s raf and py<
MISSING TERM AFTER PY<
Operators must be followed by a search term, L-number, or query name.

=> s raf and py<1990
   3 FILES SEARCHED...
   5 FILES SEARCHED...
   8 FILES SEARCHED...
L5         2469 RAF AND PY<1990

=> s bonner, ?/au
L6        13106 BONNER, ?/AU

=> s l5 and l6
L7           71 L5 AND L6

=> dup rem l7
PROCESSING COMPLETED FOR L7
L8            21 DUP REM L7 (50 DUPLICATES REMOVED)

=> s l8 and angiogenesis
L9            0 L8 AND ANGIOGENESIS

=> d 1-10
L9 HAS NO ANSWERS
'1-10 ' IS NOT A VALID SEARCH STATUS KEYWORD
Search status keywords:
NONE ---- Display only the number of postings.
STATUS -- Display statistics of the search.
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'D L74 1-10' IS NOT A VALID SEARCH STATUS KEYWORD
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STATUS -- Display statistics of the search.
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L5          2469 SEA RAF AND PY<1990
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L6 13106 SEA BONNER, ?/AU
L7 71 SEA L5 AND L6
L8 21 DUP REM L7 (50 DUPLICATES REMOVED)
L9 0 SEA L8 AND ANGIOGENESIS

=> d l8 1-10

L8 ANSWER 1 OF 21 MEDLINE DUPLICATE 1
AN 88240309 MEDLINE
DN 88240309 PubMed ID: 2837178
TI Expression of human c-**raf**-1 oncogene proteins in E. coli.
AU Kolch W; **Bonner T I**; Rapp U R
CS Laboratory of Viral Carcinogenesis, National Cancer Institute, Frederick, Maryland 21701-1013.
SO BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, **(1988 May 16)** 152 (3) 1045-9.
Journal code: 0372516. ISSN: 0006-291X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198806
ED Entered STN: 19900308
Last Updated on STN: 19980206
Entered Medline: 19880624

L8 ANSWER 2 OF 21 MEDLINE DUPLICATE 2
AN 87146380 MEDLINE
DN 87146380 PubMed ID: 3029685
TI The complete coding sequence of the human A-**raf**-1 oncogene and transforming activity of a human A-**raf** carrying retrovirus.
AU Beck T W; Huleihel M; Gunnell M; **Bonner T I**; Rapp U R
NC NO1-CO-23910 (NCI)
SO NUCLEIC ACIDS RESEARCH, **(1987 Jan 26)** 15 (2) 595-609.
Journal code: 0411011. ISSN: 0305-1048.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-X04790
EM 198704
ED Entered STN: 19900303
Last Updated on STN: 19970203
Entered Medline: 19870413

L8 ANSWER 3 OF 21 MEDLINE DUPLICATE 3
AN 86233347 MEDLINE
DN 86233347 PubMed ID: 3520560
TI Actively transcribed genes in the **raf** oncogene group, located on the X chromosome in mouse and human.
AU Huebner K; ar-Rushdi A; Griffin C A; Isobe M; Kozak C; Emanuel B S; Nagarajan L; Cleveland J L; **Bonner T I**; Goldsborough M D; +
NC CA09485 (NCI)
CA10815 (NCI)
CA21124 (NCI)
+
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, **(1986 Jun)** 83 (11) 3934-8.
Journal code: 7505876. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198607
ED Entered STN: 19900321
Last Updated on STN: 19970203
Entered Medline: 19860709

L8 ANSWER 4 OF 21 MEDLINE DUPLICATE
AN 87064566 MEDLINE
DN 87064566 PubMed ID: 3491291
TI Characterization of murine A-**raf**, a new oncogene related to the v-**raf** oncogene.
AU Huleihel M; Goldsborough M; Cleveland J; Gunnell M; **Bonner T**; Rapp U R
NC NO1-CO-23910 (NCI)
SO MOLECULAR AND CELLULAR BIOLOGY, **(1986 Jul)** 6 (7) 2655-62.
Journal code: 8109087. ISSN: 0270-7306.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-M13071
EM 198701
ED Entered STN: 19900302
Last Updated on STN: 19970203
Entered Medline: 19870120

L8 ANSWER 5 OF 21 MEDLINE DUPLICATE 5
AN 86120351 MEDLINE
DN 86120351 PubMed ID: 3003687
TI The complete coding sequence of the human **raf** oncogene and the corresponding structure of the c-**raf**-1 gene.
AU **Bonner T I**; Oppermann H; Seeburg P; Kerby S B; Gunnell M A; Young A C; Rapp U R
SO NUCLEIC ACIDS RESEARCH, **(1986 Jan 24)** 14 (2) 1009-15.
Journal code: 0411011. ISSN: 0305-1048.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-X03484
EM 198603
ED Entered STN: 19900321
Last Updated on STN: 19900321
Entered Medline: 19860321

L8 ANSWER 6 OF 21 MEDLINE DUPLICATE 6
AN 85295973 MEDLINE
DN 85295973 PubMed ID: 2993863
TI Structure and biological activity of human homologs of the **raf** /mil oncogene.
AU **Bonner T I**; Kerby S B; Sutrave P; Gunnell M A; Mark G; Rapp U R
SO MOLECULAR AND CELLULAR BIOLOGY, **(1985 Jun)** 5 (6) 1400-7.
Journal code: 8109087. ISSN: 0270-7306.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-L00206; GENBANK-L00207; GENBANK-L00208; GENBANK-L00209; GENBANK-L00210; GENBANK-L00211; GENBANK-L00212; GENBANK-L00213; GENBANK-M11376; GENBANK-M11377
EM 198509
ED Entered STN: 19900320
Last Updated on STN: 19970203
Entered Medline: 19850930

L8 ANSWER 7 OF 21 MEDLINE DUPLICATE 7
AN 85230538 MEDLINE
DN 85230538 PubMed ID: 4006904
TI Integration of transfected LTR sequences into the c-**raf** proto-oncogene: activation by promoter insertion.
AU Molders H; Defesche J; Muller D; **Bonner T I**; Rapp U R; Muller R
SO EMBO JOURNAL, **(1985 Mar)** 4 (3) 693-8.
Journal code: 8208664. ISSN: 0261-4189.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)

LA English
FS Priority Journals
EM 198508
ED Entered STN: 19900320
Last Updated on STN: 19970203
Entered Medline: 19850806

L8 ANSWER 8 OF 21 LIFESCI COPYRIGHT 2003 CSA
AN 85:19016 LIFESCI
TI Integration of transfected LTR sequences into the c-**raf** proto-oncogene: Activation by promoter insertion.
AU Moelders, H.; Defesche, J.; Mueller, D.; **Bonner, T.I.**; Rapp, U.R.; Mueller, R.
CS Eur. Mol. Biol. Lab., Postfach 10,2209, D-6900 Heidelberg, FRG
SO EMBO J., (**1985**) vol. 4, no. 3, pp. 693-698.
DT Journal
FS G; N
LA English
SL English

L8 ANSWER 9 OF 21 HCAPLUS COPYRIGHT 2003 ACS
AN 1986:565931 HCAPLUS
DN 105:165931
TI The **raf** oncogene
AU Rapp, U. R.; **Bonner, T. I.**; Cleveland, J. L.
CS Lab. Viral Carcinog., Natl. Cancer Inst., Frederick, MD, 21701, USA
SO Retroviruses Hum. Pathol., Int. Symp. (**1985**), Meeting Date 1984, 449-72. Editor(s): Gallo, Robert C.; Stehelin, Dominique; Varnier, Oliviero E. Publisher: Humana, Clifton, N. J.
CODEN: 55FGA7
DT Conference; General Review
LA English

L8 ANSWER 10 OF 21 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 8
AN 1986:56497 BIOSIS
DN BR30:56497
TI GENES AND GENE PRODUCTS INVOLVED IN GROWTH REGULATION OF TUMOR CELLS.
AU RAPP U R; **BONNER T I**; MOELLING K; JANSEN H W; BISTER K; IHLE J
CS LAB. OF VIRAL CARCINOGENESIS, NATL. CANCER INST., FREDERICK CANCER RES. FACILITY, FREDERICK, MD. 21701, USA.
SO HAVEMANN, K., G. SORENSON AND C. GROPP (ED.). RECENT RESULTS IN CANCER RESEARCH, 99. PEPTIDE HORMONES IN LUNG CANCER; MEETING, MARBURG, WEST GERMANY, JUNE 18-20, 1984. XII+248P. SPRINGER-VERLAG NEW YORK, INC.: SECAUCUS, N.J., USA; BERLIN, WEST GERMANY. ILLUS. (1985) 0 (0), 221-236.
CODEN: RRCRBU. ISSN: 0080-0015. ISBN: 0-387-15504-X, 3-540-15504-X.
FS BR; OLD
LA English

=> d 11-20
L9 HAS NO ANSWERS
'11-20 ' IS NOT A VALID SEARCH STATUS KEYWORD
Search status keywords:
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L5 2469 SEA RAF AND PY<1990
L6 13106 SEA BONNER, ?/AU
L7 71 SEA L5 AND L6
L8 21 DUP REM L7 (50 DUPLICATES REMOVED)
L9 0 SEA L8 AND ANGIOGENESIS

=> d l8 11-20

L8 ANSWER 11 OF 21 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 1985:164060 BIOSIS
DN BR29:54056

TI STRUCTURE AND TRANSCRIPTION OF THE C-**RAF**-1 ONCOGENE LOCUS.
AU CLEVELAND J L; **BONNER T I**; GOLDSBOROUGH M D; RAPP U R
CS NATL. CANCER INST., FREDERICK CANCER RES. FACILITY, FREDERICK, MD. 21701.
SO SYMPOSIUM ON BIOCHEMICAL AND MOLECULAR EPIDEMIOLOGY OF CANCER HELD AT THE 14TH ANNUAL MEETING OF THE UCLA (UNIVERSITY OF CALIFORNIA-LOS ANGELES) SYMPOSIA ON MOLECULAR AND CELLULAR BIOLOGY, APR. 6-13, 1985. J CELL BIOCHEM SUPPL. (1985) 0 (9 PART C), 26.
CODEN: JCBSD7.
DT Conference
FS BR; OLD
LA English

L8 ANSWER 12 OF 21 SCISEARCH COPYRIGHT 2003 ISI (R)
AN 84:1206 SCISEARCH
GA The Genuine Article (R) Number: RV308
TI 2 HUMAN HOMOLOGS TO A NEW RETROVIRAL ONCOGENE **RAF**-1 AND **RAF**-2 ARE ASSIGNED TO HUMAN CHROMOSOME-3 AND CHROMOSOME-4, RESPECTIVELY
AU **BONNER T I (Reprint)**; RAPP U R; NASH W G; OBRIEN S J
CS NCI, VIRAL CARCINOGENESIS LAB, FREDERICK, MD, 21701
CYA USA
SO CYTOGENETICS AND CELL GENETICS, (**1984**) Vol. 37, No. 1-4, pp. 424.
DT Conference; Journal
FS LIFE
LA ENGLISH
REC No References

L8 ANSWER 13 OF 21 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 1984:87878 BIOSIS
DN BR27:4370
TI 2 HUMAN HOMOLOGUES TO A NEW RETROVIRAL ONCOGENE **RAF**-1 AND **RAF**-2 ARE ASSIGNED TO HUMAN CHROMOSOMES 3 AND 4 RESPECTIVELY.
AU **BONNER T I**; RAPP U R; NASH W G; O'BRIEN S J
CS LAB. VIRAL CARCINOGENESIS, NATL. CANCER INST., FREDERICK, MD 21701.
SO 7TH INTERNATIONAL WORKSHOP ON HUMAN GENE MAPPING, LOS ANGELES, CALIF., USA, AUG. 21-26, 1983. CYTOGENET CELL GENET. (1984) 37 (1-4), 424.
CODEN: CGCGBR. ISSN: 0301-0171.
DT Conference
FS BR; OLD
LA English

L8 ANSWER 14 OF 21 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 9
AN 1985:67459 BIOSIS
DN BR28:67459
TI THE MIL-**RAF** ONCOGENE.
AU BISTER K; LURZ R; JANSEN H W; SUTRAVE P; **BONNER T I**; RAPP U R
CS OTTO-WARBURG-LAB., MAX-PLANCK-INST. FUER MOLEKULARE GENETIK, D-1000 BERLIN 33, FRG.
SO BISHOP, J. M., J. D. ROWLEY AND M. GREAVES (ED.). UCLA (UNIVERSITY OF CALIFORNIA LOS ANGELES) SYMPOSIA ON MOLECULAR AND CELLULAR BIOLOGY NEW SERIES, VOL. 17. GENES AND CANCER; MEETING, STEAMBOAT-SPRINGS, COLO., USA, MAR. 11-17, 1984. XXII+687P. ALAN R. LISS, INC.: NEW YORK, N.Y., USA. ILLUS. (1984) 0 (0), 315-328.
CODEN: USMBD6. ISSN: 0735-9543. ISBN: 0-8451-2616-4.
FS BR; OLD
LA English

L8 ANSWER 15 OF 21 MEDLINE DUPLICATE 10
AN 84117458 MEDLINE
DN 84117458 PubMed ID: 6319999
TI Homologous cell-derived oncogenes in avian carcinoma virus MH2 and murine sarcoma virus 3611.
AU Jansen H W; Lurz R; Bister K; **Bonner T I**; Mark G E; Rapp U R
SO NATURE, **(1984 Jan 19-25)** 307 (5948) 281-4.
Journal code: 0410462. ISSN: 0028-0836.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)

LA English
FS Priority Journals
EM 198403
ED Entered STN: 19900319
Last Updated on STN: 19970203
Entered Medline: 19840302

L8 ANSWER 16 OF 21 MEDLINE DUPLICATE 11
AN 84191511 MEDLINE
DN 84191511 PubMed ID: 6325930
TI Nucleotide sequence of avian retroviral oncogene v-mil: homologue of murine retroviral oncogene v-**raf**.
AU Sutrave P; **Bonner T I**; Rapp U R; Jansen H W; Patschinsky T; Bister K
SO NATURE, **(1984 May 3-9)** 309 (5963) 85-8.
Journal code: 0410462. ISSN: 0028-0836.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-K02082
EM 198406
ED Entered STN: 19900319
Last Updated on STN: 19970203
Entered Medline: 19840620

L8 ANSWER 17 OF 21 MEDLINE DUPLICATE 12
AN 84097515 MEDLINE
DN 84097515 PubMed ID: 6691137
TI The human homologs of the **raf** (mil) oncogene are located on human chromosomes 3 and 4.
AU **Bonner T**; O'Brien S J; Nash W G; Rapp U R; Morton C C; Leder P
SO SCIENCE, **(1984 Jan 6)** 223 (4631) 71-4.
Journal code: 0404511. ISSN: 0036-8075.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198402
ED Entered STN: 19900319
Last Updated on STN: 19900319
Entered Medline: 19840214

L8 ANSWER 18 OF 21 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 1984:129333 BIOSIS
DN BR27:45825
TI THE HUMAN CELLULAR HOMOLOGUES OF THE **RAF**-MIL ONCOGENE.
AU SUTRAVE P; GEORGE M; **BONNER T**
CS NCI/NIH, FREDERICK, MD 21701.
SO SYMPOSIUM ON GENES AND CANCER HELD AT THE 13TH ANNUAL UCLA (UNIVERSITY OF CALIFORNIA - LOS ANGELES) SYMPOSIA, LOS ANGELES, CALIF., USA, FEB. 11-17, 1984. J CELL BIOCHEM. (1984) 0 (8 PART A), 70.
CODEN: JCBSD7.
DT Conference
FS BR; OLD
LA English

L8 ANSWER 19 OF 21 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 1984:135716 BIOSIS
DN BR27:52208
TI THE **RAF** ONCOGENE NUCLEIC-ACID SEQUENCE EVOLUTION AND REQUIRED STRUCTURES FOR TRANSFORMATION.
AU MARK G E; GOLDSBOROUGH M D; **BONNER T I**; RAPP U R
CS NATIONAL CANCER INST., FREDERICK, MD 21701.
SO SYMPOSIUM ON GENES AND CANCER HELD AT THE 13TH ANNUAL UCLA (UNIVERSITY OF CALIFORNIA - LOS ANGELES) SYMPOSIA, LOS ANGELES, CALIF., USA, FEB. 11-17, 1984. J CELL BIOCHEM. (1984) 0 (8 PART A), 63.
CODEN: JCBSD7.
DT Conference

FS BR; OLD
LA English

L8 ANSWER 20 OF 21 MEDLINE DUPLICATE 13
AN 83273593 MEDLINE
DN 83273593 PubMed ID: 6308607
TI Structure and biological activity of v-**raf**, a unique oncogene transduced by a retrovirus.
AU Rapp U R; Goldsborough M D; Mark G E; **Bonner T I**; Groffen J; Reynolds F H Jr; Stephenson J R
NC NO1-CO-75380 (NCI)
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, **(1983 Jul)** 80 (14) 4218-22.
    Journal code: 7505876. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198309
ED Entered STN: 19900319
    Last Updated on STN: 19970203
    Entered Medline: 19830909

=> d l8 20 ab

L8 ANSWER 20 OF 21 MEDLINE DUPLICATE 13
AB We have molecularly cloned a unique acutely transforming replication-defective mouse type C virus (3611-MSV) and characterized its acquired oncogene. The viral genome closely resembles Moloney (M) murine leukemia virus (MuLV), except for a substitution in M-MuLV in the middle of p30 and the middle of the polymerase gene (pol). Heteroduplex analysis revealed that 2.4 kilobases of M-MuLV DNA were replaced by 1.2 kilobases of cellular DNA. The junctions between viral and cellular sequences were determined by DNA sequence analysis to be 517 nucleotides into the p30 sequence and 1,920 nucleotides into the polymerase sequence. Comparison of the transforming gene from 3611-MSV, designated v-**raf**, with previously isolated retrovirus oncogenes either by direct hybridization or by comparison of restriction fragments of their cellular homologs shows it to be unique. Transfection of NIH 3T3 cells with cloned 3611-MSV proviral DNA leads to highly efficient transformation and the recovered virus elicits tumors in mice typical of the 3611-MSV virus. Transfected NIH 3T3 cells express two 3611-MSV-specific polyproteins (P75 and P90), both of which contain NH2-terminal gag gene-encoded components linked to the acquired sequence (v-**raf**) translational product. The cellular homolog, c-**raf**, is present in one or two copies per haploid genome in mouse and human DNA.

=> dis his

    (FILE 'HOME' ENTERED AT 16:47:37 ON 21 FEB 2003)

    FILE 'MEDLINE, SCISEARCH, LIFESCI, BIOTECHDS, BIOSIS, EMBASE, HCAPLUS, NTIS, ESBIOBASE, BIOTECHNO, WPIDS' ENTERED AT 16:47:48 ON 21 FEB 2003
L1 84 S RAF-CAAX
L2 3 S L1 AND ANGIOGENE?
L3 2 DUP REM L2 (1 DUPLICATE REMOVED)
L4 0 S L1 AND PY<1990
L5 2469 S RAF AND PY<1990
L6 13106 S BONNER, ?/AU
L7 71 S L5 AND L6
L8 21 DUP REM L7 (50 DUPLICATES REMOVED)
L9 0 S L8 AND ANGIOGENESIS

=> log h
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NEWS 5	Apr 19	US Patent Applications available in IFICDB, IFIPAT, and IFIUDB
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NEWS 7	Apr 22	BIOSIS Gene Names now available in TOXCENTER
NEWS 8	Apr 22	Federal Research in Progress (FEDRIP) now available
NEWS 9	Jun 03	New e-mail delivery for search results now available
NEWS 10	Jun 10	MEDLINE Reload
NEWS 11	Jun 10	PCTFULL has been reloaded
NEWS 12	Jul 02	FOREGE no longer contains STANDARDS file segment
NEWS 13	Jul 22	USAN to be reloaded July 28, 2002; saved answer sets no longer valid
NEWS 14	Jul 29	Enhanced polymer searching in REGISTRY
NEWS 15	Jul 30	NETFIRST to be removed from STN
NEWS 16	Aug 08	CANCERLIT reload
NEWS 17	Aug 08	PHARMAMarketLetter(PHARMAML) - new on STN
NEWS 18	Aug 08	NTIS has been reloaded and enhanced
NEWS 19	Aug 19	Aquatic Toxicity Information Retrieval (AQUIRE) now available on STN
NEWS 20	Aug 19	IFIPAT, IFICDB, and IFIUDB have been reloaded
NEWS 21	Aug 19	The MEDLINE file segment of TOXCENTER has been reloaded
NEWS 22	Aug 26	Sequence searching in REGISTRY enhanced
NEWS 23	Sep 03	JAPIO has been reloaded and enhanced
NEWS 24	Sep 16	Experimental properties added to the REGISTRY file
NEWS 25	Sep 16	CA Section Thesaurus available in CAPLUS and CA
NEWS 26	Oct 01	CASREACT Enriched with Reactions from 1907 to 1985
NEWS 27	Oct 21	EVENTLINE has been reloaded
NEWS 28	Oct 24	BEILSTEIN adds new search fields
NEWS 29	Oct 24	Nutraceuticals International (NUTRACEUT) now available on STN
NEWS 30	Oct 25	MEDLINE SDI run of October 8, 2002
NEWS 31	Nov 18	DKILIT has been renamed APOLLIT
NEWS 32	Nov 25	More calculated properties added to REGISTRY
NEWS 33	Dec 02	TIBKAT will be removed from STN
NEWS 34	Dec 04	CSA files on STN
NEWS 35	Dec 17	PCTFULL now covers WP/PCT Applications from 1978 to date
NEWS 36	Dec 17	TOXCENTER enhanced with additional content
NEWS 37	Dec 17	Adis Clinical Trials Insight now available on STN
NEWS 38	Dec 30	ISMEC no longer available
NEWS 39	Jan 13	Indexing added to some pre-1967 records in CA/CAPLUS
NEWS 40	Jan 21	NUTRACEUT offering one free connect hour in February 2003
NEWS 41	Jan 21	PHARMAML offering one free connect hour in February 2003
NEWS 42	Jan 29	Simultaneous left and right truncation added to COMPENDEX, ENERGY, INSPEC
NEWS 43	Feb 13	CANCERLIT is no longer being updated

NEWS EXPRESS	January 6 CURRENT WINDOWS VERSION IS V6.01a, CURRENT MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP), AND CURRENT DISCOVER FILE IS DATED 01 OCTOBER 2002
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 NEWS WWW      CAS World Wide Web Site (general information)

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=> s raf
L1        29774 RAF

=> s l1 (10a) angiogene?
L2           37 L1 (10A) ANGIOGENE?

=> dup rem l2
PROCESSING COMPLETED FOR L2
L3           10 DUP REM L2 (27 DUPLICATES REMOVED)

=> d 1-10
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L3 ANSWER 1 OF 10 HCAPLUS COPYRIGHT 2003 ACS DUPLICATE 1
AN 2002:483067 HCAPLUS
DN 137:57540
TI Antisense oligonucleotide inhibition of raf gene expression for treatment of cancer
IN Monia, Brett P.
PA Isis Pharmaceuticals, Inc., USA
SO U.S., 41 pp., Cont.-in-part of U. S. 6,090,626.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 9

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6410518	B1	20020625	US 2000-506073	20000218
	US 5563255	A	19961008	US 1994-250856	19940531
	WO 9532987	A1	19951207	WO 1995-US7111	19950531
	W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KG, KP, KR, KZ, LK, LR, LT, LV, MD, MG, MN, MX, NO, NZ, PL, PT, RO, RU, SI, SK, TJ, TT, UA, US, UZ, VN				
	RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	US 5952229	A	19990914	US 1996-756806	19961126
	US 5981731	A	19991109	US 1997-888982	19970707
	WO 9902167	A1	19990121	WO 1998-US13961	19980706
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	US 6090626	A	20000718	US 1998-143214	19980828
	JP 2000152797	A2	20000606	JP 2000-8654	20000118
	JP 09507502	T2	19970729		
	JP 3121599	B2	20010109		
	US 2003032607	A1	20030213	US 2002-57550	20020125
PRAI	US 1994-250856	A1	19940531		
	WO 1995-US7111	A1	19950531		
	US 1996-756806	A1	19961126		
	US 1997-888982	A2	19970707		
	WO 1998-US13961	A2	19980706		
	US 1998-143214	A2	19980828		
	JP 1996-501257	A3	19950531		
	US 2000-506073	A1	20000218		

RE.CNT 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 10 HCAPLUS COPYRIGHT 2003 ACS
AN 2002:256057 HCAPLUS
DN 136:274281
TI Raf proteins, cDNA sequences, agonists or antagonists and uses thereof in therapy and diagnosis of endothelium affected diseases
IN Hatzopoulos, Antonis; Hautmann, Martina; Herbst, Myriam; Geishauser, Albert; Schoch, Juergen
PA GSF-Forschungszentrum fuer Umwelt und Gesundheit G.m.b.H., Germany
SO PCT Int. Appl., 64 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002026246	A2	20020404	WO 2001-EP11282	20010928
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,				

GM, HR, HU, ID, IL, , IS, JP, KE, KG, KP, KR, KZ, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL,
PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG,
US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2002023571 A5 20020408 AU 2002-23571 20010928
PRAI EP 2000-121490 A 20000929
EP 2000-2000121490A 20000929
WO 2001-EP11282 W 20010928

L3 ANSWER 3 OF 10 MEDLINE DUPLICATE 2
AN 2002346607 MEDLINE
DN 22084557 PubMed ID: 12089446
TI Tumor regression by targeted gene delivery to the neovasculature.
CM Comment in: Science. 2002 Jun 28;296(5577):2314-5
AU Hood John D; Bednarski Mark; Frausto Ricardo; Guccione Samira; Reisfeld Ralph A; Xiang Rong; Cheresh David A
CS Department of Immunology, The Scripps Research Institute, 10550 North Torrey Pines Road, La Jolla, CA 92037, USA.
NC CA50286 (NCI)
P41 RR09784 (NCRR)
T32 CA09696 (NCI)
SO SCIENCE, (2002 Jun 28) 296 (5577) 2404-7.
Journal code: 0404511. ISSN: 1095-9203.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200207
ED Entered STN: 20020629
Last Updated on STN: 20020724
Entered Medline: 20020723

L3 ANSWER 4 OF 10 MEDLINE DUPLICATE 3
AN 2002195082 MEDLINE
DN 21925512 PubMed ID: 11927284
TI Unraveling the complexities of the Raf/MAP kinase pathway for pharmacological intervention.
CM Erratum in: Trends Mol Med 2002 May;8(5):243
AU Herrera Roman; Sebolt-Leopold Judith S
CS Department of Cancer Molecular Sciences, Pfizer Global Research & Development, Ann Arbor Laboratories, 2800 Plymouth Road, Ann Arbor, MI 48105, USA.
SO Trends Mol Med, (2002) 8 (4 Suppl) S27-31. Ref: 30
Journal code: 100966035. ISSN: 1471-4914.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200208
ED Entered STN: 20020404
Last Updated on STN: 20021211
Entered Medline: 20020819

L3 ANSWER 5 OF 10 Elsevier BIOBASE COPYRIGHT 2003 Elsevier Science B.V.
DUPLICATE
AN 2002087122 ESBIOBASE
TI Unraveling the complexities of the Raf/MAP kinase pathway for pharmacological intervention
AU Herrera R.; Sebolt-Leopold J.S.
CS R. Herrera, Dept. of Cancer Molecular Sciences, Pfizer Global Research/Development, Ann Arbor Laboratories, 2800 Plymouth Road, Ann Arbor, MI 48105, United States.
E-mail: judith.leopold@pfizer.com
SO Trends in Molecular Medicine, (2002), 8/4 SUPPL. (S27-S31), 30

reference(s)
CODEN: TMMRCY ISSN: 1471-4914
PUI S1471491402023079
DT Journal; General Review
CY United Kingdom
LA English
SL English

L3 ANSWER 6 OF 10 HCAPLUS COPYRIGHT 2003 ACS DUPLICATE 5
AN 2001:137041 HCAPLUS
DN 134:188193
TI Protein and cDNA sequences of modified human protein kinase C-Raf and/or H-Ras and therapeutic uses thereof for modulation of angiogenesis
IN Hood, John; Eliceiri, Brian; Cheresh, David A.
PA The Scripps Research Institute, USA
SO PCT Int. Appl., 102 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001012210	A1	20010222	WO 2000-US21842	20000811
WO 2001012210	C2	20020912		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1210099	A1	20020605	EP 2000-955423	20000811
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
NO 2002000718	A	20020410	NO 2002-718	20020212
PRAI US 1999-148924P	P	19990813		
US 2000-215951P	P	20000705		
WO 2000-US21842	W	20000811		

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 7 OF 10 MEDLINE DUPLICATE 6
AN 2000120713 MEDLINE
DN 20120713 PubMed ID: 10655059
TI A genome-wide survey of RAS transformation targets.
AU Zuber J; Tchernitsa O I; Hinzmann B; Schmitz A C; Grips M; Hellriegel M; Sers C; Rosenthal A; Schafer R
CS [1] Laboratory of Molecular Tumour Pathology, Institute of Pathology, Charite, Humboldt-University D-10117, Berlin, Germany.
SO NATURE GENETICS, (2000 Feb) 24 (2) 144-52.
Journal code: 9216904. ISSN: 1061-4036.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-AB000220; GENBANK-AF023451; GENBANK-AF058922; GENBANK-AF061749; GENBANK-AF131207; GENBANK-AF141386; GENBANK-D38496; GENBANK-E08769; GENBANK-L11932; GENBANK-NM004398; GENBANK-U17032; GENBANK-U79550; GENBANK-X65627; GENBANK-Z29651
EM 200002
ED Entered STN: 20000314
Last Updated on STN: 20000314
Entered Medline: 20000228

L3 ANSWER 8 OF 10 MEDLINE DUPLICATE 7
AN 1999067717 MEDLINE
DN 99067717 PubMed ID: 9850731

TI Inhibitory effect of theobr[redacted]ne on induction of **angiogenesi**[redacted]
and VEGF mRNA expression in v-**raf** transfectants of human
urothelial cells HCV-29.
AU Skopinska-Rozewska E; Janik P; Przybyszewska M; Sommer E; Bialas-Chromiec
B
CS Department of Immunology, National Institute of Tuberculosis and Lung
Diseases, Warsaw, Poland.
SO INTERNATIONAL JOURNAL OF MOLECULAR MEDICINE, (1998 Dec) 2 (6) 649-52.
Journal code: 9810955. ISSN: 1107-3756.
CY Greece
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199901
ED Entered STN: 19990115
Last Updated on STN: 20000303
Entered Medline: 19990107

L3 ANSWER 9 OF 10 MEDLINE DUPLICATE 8
AN 1999066573 MEDLINE
DN 99066573 PubMed ID: 9851248
TI Angiogenesis induced by urothelial cells (HCV-29) and their v-ras and
v-raf transfectants.
AU Przybyszewska M; Miloszewska J; Janik P
CS Department of Cell Biology, The Maria Sklodowska-Curie Cancer Center,
Warsaw, Poland.
SO CANCER LETTERS, (1998 Sep 25) 131 (2) 157-61.
Journal code: 7600053. ISSN: 0304-3835.
CY Ireland
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199812
ED Entered STN: 19990115
Last Updated on STN: 19990115
Entered Medline: 19981221

L3 ANSWER 10 OF 10 HCAPLUS COPYRIGHT 2003 ACS
AN 1997:617993 HCAPLUS
DN 127:272793
TI Antiproliferative combinations, containing raf-targeted oligonucleotides
and chemotherapeutic compounds
IN Muller, Marcel; Geiger, Thomas; Altmann, Karl-Heinz; Fabbro, Doriano;
Monia, Brett
PA Novartis AG, Switz.
SO PCT Int. Appl., 118 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9732604	A1	19970912	WO 1997-EP875	19970224
	W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, HU, IL, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9720925	A1	19970922	AU 1997-20925	19970224
	ZA 9701936	A	19970908	ZA 1997-1936	19970306
PRAI	US 1996-612787	A	19960307		
	WO 1997-EP875	W	19970224		

=> d 8-10 ab

L3 ANSWER 8 OF 10 MEDLINE DUPLICATE 7
AB Neovascularisation plays a crucial role in solid tumor growth and

metastasis formation. Our previous studies showed that theophylline and theobromine suppressed cutaneous neovascular reaction induced in mice by human blood leukocytes, and lung as well as ovarian cancer cells. Here, we investigated the in vivo effect of theobromine on angiogenic activity of human urothelial cell line HCV-29, v-raf transfected (mouse cutaneous assay), and the in vitro effect of this drug on VEGF, tPA, uPA and PAI mRNA expression in these cells (RT-PCR method). Theobromine suppressed **angiogenesis** induced in mice by HCV-29-v-**raf** cells, inhibited VEGF mRNA expression, and had no effect on transcription of uPA and tPA in these cells. HCV-29-v-raf transfectants do not display transcripts of PAI, in the presence or the absence of theobromine.

L3 ANSWER 9 OF 10 MEDLINE DUPLICATE 8
AB The angiogenic ability of human urothelial cells (HCV-29) and their v-ras and v-**raf** transfectants was studied. The most pronounced **angiogenesis**, observed in vivo, induced v-**raf** -transfected cells. The lowest degree of induction of neovascularization presented cells of the parental line. The increased extent of angiogenesis correlated with the presence of VEGF mRNA as measured by RT-PCR as well as the level of VEGF as visualized by the method of Western blotting.

L3 ANSWER 10 OF 10 HCAPLUS COPYRIGHT 2003 ACS
AB The invention relates to combinations of raf-targeted (esp. c-raf-targeted) deoxyribo- and ribo-oligonucleotides and derivs. thereof with other chemotherapeutic compds., as well as to pharmaceutical prepns. and/or therapies, in relation to disease states which respond to such oligonucleotides or oligonucleotide derivs., esp. to modulation of the activity of a regulatory protein. In particular, the invention relates to products or combinations comprising antisense oligonucleotides or oligonucleotide derivs. targeted to nucleic acids encoding raf and other (preferably std.) chemotherapeutics, either in fixed combination or for chronol. staggered or simultaneous administration, and the combined use of both classes of compds., either in fixed combination or for chronol. staggered or simultaneous administration, for the treatment of proliferative diseases, esp. tumor diseases, that can be treated by inhibition of raf activity, i.e., where the antisense oligonucleotides or oligonucleotide derivs. are targeted to nucleic acids encoding the regulatory protein raf or active mutated derivs. thereof.

=> d 8-10 kwic

L3 ANSWER 8 OF 10 MEDLINE DUPLICATE 7
TI Inhibitory effect of theobromine on induction of **angiogenesis** and VEGF mRNA expression in v-**raf** transfectants of human urothelial cells HCV-29.
AB . . . vitro effect of this drug on VEGF, tPA, uPA and PAI mRNA expression in these cells (RT-PCR method). Theobromine suppressed **angiogenesis** induced in mice by HCV-29-v-**raf** cells, inhibited VEGF mRNA expression, and had no effect on transcription of uPA and tPA in these cells. HCV-29-v-raf transfectants. . .

L3 ANSWER 9 OF 10 MEDLINE DUPLICATE 8
AB The angiogenic ability of human urothelial cells (HCV-29) and their v-ras and v-**raf** transfectants was studied. The most pronounced **angiogenesis**, observed in vivo, induced v-**raf** -transfected cells. The lowest degree of induction of neovascularization presented cells of the parental line. The increased extent of angiogenesis correlated. . .

L3 ANSWER 10 OF 10 HCAPLUS COPYRIGHT 2003 ACS
IT Alkylating agents, biological
Angiogenesis inhibitors
Antitumor agents
Chemotherapy
Drug delivery systems
Fibrosis
Hyperplasia
Immunomodulators

Psoriasis
Vaccines
(**raf**-targeted oligonucleotide-chemotherapeutic compd. antiproliferative combinations)

=> d 1-8 ab

L3 ANSWER 1 OF 10 HCAPLUS COPYRIGHT 2003 ACS DUPLICATE 1
AB Oligonucleotides are provided which are targeted to nucleic acids encoding human raf and capable of inhibiting raf expression. The oligonucleotides may have chem. modifications at one or more positions and may be chimeric oligonucleotides. Methods of inhibiting the expression of human raf using oligonucleotides of the invention are also provided. The present invention further comprises methods of inhibiting hyperproliferation of cells and methods of treating or preventing conditions, including hyperproliferative conditions, assocd. with raf expression.

L3 ANSWER 2 OF 10 HCAPLUS COPYRIGHT 2003 ACS
AB Disclosed are pharmaceutical compns. comprising polynucleotides encoding a Raf protein, vectors, host cells, polypeptides encoded by said polynucleotides as well as agonists or antagonists thereof. As a preferred embodiment, the above mentioned Raf protein is B-Raf. Furthermore, described are uses of such pharmaceutical compns. for preventing or treating pathol. conditions in which endothelial cells are involved or affected. Finally, methods for screening compds. acting as agonists or antagonists as well as diagnostic compns. and methods are disclosed. It was found by inventors that in a mouse embryonic endothelial stem cell line in wich B-Raf gene is inactivated, the expression profile of a large set of genes is altered compared to the corresponding wild-type (wt) cells. These results were confirmed in vivo by comparing gene expression profiles on B-Raf null mutant embryos. The results show that genes, whose expression changed in the B-Raf null cells, were affected during embryonic vascular development. The similarity to the angiogenin 1 null mutant mice phenotype obsd., which points at a position of B-Raf downstream from tie-2 in the signaling cascade, substantiates the role of B-**Raf** in **angiogenesis**, wound healing and endothelial cell migration.

L3 ANSWER 3 OF 10 MEDLINE DUPLICATE 2
AB Efforts to influence the biology of blood vessels by gene delivery have been hampered by a lack of targeting vectors specific for endothelial cells in diseased tissues. Here we show that a cationic nanoparticle (NP) coupled to an integrin alphavbeta3-targeting ligand can deliver genes selectively to angiogenic blood vessels in tumor-bearing mice. The therapeutic efficacy of this approach was tested by generating NPs conjugated to a mutant **Raf** gene, ATPmu-**Raf**, which blocks endothelial signaling and **angiogenesis** in response to multiple growth factors. Systemic injection of the NP into mice resulted in apoptosis of the tumor-associated endothelium, ultimately leading to tumor cell apoptosis and sustained regression of established primary and metastatic tumors.

L3 ANSWER 4 OF 10 MEDLINE DUPLICATE 3
AB The Ras-MAP kinase pathway has attracted much attention from academic and pharmaceutical laboratories because of its central role in regulating tumor cell growth and survival, differentiation and **angiogenesis**. Although the central players in this pathway -Ras, **Raf**, and MEK - have been well studied, how best to exploit them for therapeutic gain has eluded oncology researchers in the past. Several small-molecule inhibitors that target specific steps of the MAP kinase cascade have recently entered the clinical arena. While we await answers on their ultimate therapeutic use, the availability of translational assays for monitoring target suppression will no doubt play a significant role in optimizing our chances of success.

L3 ANSWER 5 OF 10 Elsevier BIOBASE COPYRIGHT 2003 Elsevier Science B.V.
DUPLICATE
AB The Ras-MAP kinase pathway has attracted much attention from academic and

pharmaceutical laboratories because of its central role in regulating tumor cell growth and survival, differentiation and **angiogenesis**. Although the central players in this pathway - Ras, **Raf**, and MEK - have been well studied, how best to exploit them for therapeutic gain has eluded oncology researchers in the past. Several small-molecule inhibitors that target specific steps of the MAP kinase cascade have recently entered the clinical arena. While we await answers on their ultimate therapeutic use, the availability of translational assays for monitoring target suppression will no doubt play a significant role in optimizing our chances of success.

L3 ANSWER 6 OF 10 HCAPLUS COPYRIGHT 2003 ACS DUPLICATE 5
AB The invention provides protein and cDNA sequences of modified human protein kinase C-Raf and/or H-Ras. The present invention describes methods for modulating **angiogenesis** in tissues using **Raf** and/or Ras protein, modified **Raf** or Ras protein, and nucleic acids encoding for such. Also disclosed are three inactive mutant human C-Raf proteins including RafK375M which contains a point substitution mutation lys375met, Raf1-305 in which C-terminal residues 1-305 are deleted, and Raf306-648 in which N-terminal residues 306-648 are deleted. The invention also provides four inactive mutant human H-Ras proteins which contains substitution mutations such as RasG12V(gly12val), RasV12S35(gly12val, thr35ser), RasS17N(ser17asp) and RasV12C40(gly12val, tyr40cys). Particularly the invention describes methods for inhibiting **angiogenesis** using an inactive **Raf** and/or Ras protein, or nucleic acids encoding therefor, or for potentiating **angiogenesis** using an active **Raf** and/or Ras protein, or nucleic acids encoding therefor. The invention also describes the use of gene delivery systems for providing nucleic acids encoding for the Raf or Ras protein, or modified forms thereof.

L3 ANSWER 7 OF 10 MEDLINE DUPLICATE 6
AB An important aspect of multi-step tumorigenesis is the mutational activation of genes of the RAS family, particularly in sporadic cancers of the pancreas, colon, lung and myeloid system. RAS genes encode small GTP-binding proteins that affect gene expression in a global way by acting as major switches in signal transduction processes, coupling extracellular signals with transcription factors. Oncogenic forms of RAS are locked in their active state and transduce signals essential for transformation, **angiogenesis**, invasion and metastasis via downstream pathways involving the **RAF**/MEK/ERK cascade of cytoplasmic kinases, the small GTP-binding proteins RAC and RHO, phosphatidylinositol 3-kinase and others. We have used subtractive suppression hybridization (SSH), a PCR-based cDNA subtraction technique, to contrast differential gene expression profiles in immortalized, non-tumorigenic rat embryo fibroblasts and in HRAS- transformed cells. Sequence and expression analysis of more than 1,200 subtracted cDNA fragments revealed transcriptional stimulation or repression of 104 ESTs, 45 novel sequences and 244 known genes in HRAS- transformed cells compared with normal cells. Furthermore, we identified common and distinct targets in cells transformed by mutant HRAS, KRAS and NRAS, as well as 61 putative target genes controlled by the RAF/MEK/ERK pathway in reverted cells treated with the MEK-specific inhibitor PD 98059.

L3 ANSWER 8 OF 10 MEDLINE DUPLICATE 7
AB Neovascularisation plays a crucial role in solid tumor growth and metastasis formation. Our previous studies showed that theophylline and theobromine suppressed cutaneous neovascular reaction induced in mice by human blood leukocytes, and lung as well as ovarian cancer cells. Here, we investigated the in vivo effect of theobromine on angiogenic activity of human urothelial cell line HCV-29, v-raf transfected (mouse cutaneous assay), and the in vitro effect of this drug on VEGF, tPA, uPA and PAI mRNA expression in these cells (RT-PCR method). Theobromine suppressed **angiogenesis** induced in mice by HCV-29-v-**raf** cells, inhibited VEGF mRNA expression, and had no effect on transcription of uPA and tPA in these cells. HCV-29-v-raf transfectants do not display transcripts of PAI, in the presence or the absence of theobromine.

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NEWS 6	Aug 26	Sequence searching in REGISTRY enhanced
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NEWS 9	Sep 16	CA Section Thesaurus available in CAPLUS and CA
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NEWS 19	Jan 29	Simultaneous left and right truncation added to COMPENDEX, ENERGY, INSPEC
NEWS 20	Feb 13	CANCERLIT is no longer being updated
NEWS 21	Feb 24	METADEX enhancements
NEWS 22	Feb 24	PCTGEN now available on STN
NEWS 23	Feb 24	TEMA now available on STN
NEWS 24	Feb 26	NTIS now allows simultaneous left and right truncation
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NEWS 26	Mar 04	SDI PACKAGE for monthly delivery of multifile SDI results
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NEWS 32	Apr 17	Polymer searching in REGISTRY enhanced
NEWS 33	Jun 13	Indexing from 1947 to 1956 added to records in CA/CAPLUS
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NEWS 35	Apr 28	RDISCLOSURE now available on STN
NEWS 36	May 05	Pharmacokinetic information and systematic chemical names added to PHAR
NEWS 37	May 15	MEDLINE file segment of TOXCENTER reloaded
NEWS 38	May 15	Supporter information for ENCOMPPAT and ENCOMPLIT updated
NEWS 39	May 16	CHEMREACT will be removed from STN
NEWS 40	May 19	Simultaneous left and right truncation added to WSCA
NEWS 41	May 19	RAPRA enhanced with new search field, simultaneous left and right truncation
NEWS 42	Jun 06	Simultaneous left and right truncation added to CBNB
NEWS 43	Jun 06	PASCAL enhanced with additional data
NEWS 44	Jun 20	2003 edition of the FSTA Thesaurus is now available
NEWS 45	Jun 25	HSDB has been reloaded

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                AND CURRENT DISCOVER FILE IS DATED 01 APRIL 2003
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 => S ZHOU, ?/AU
 L1       175856 ZHOU, ?/AU

 => S L1 AND PY=1998
    8 FILES SEARCHED...
 L2        13860 L1 AND PY=1998
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=> S L2 AND RAF-ERK
L3            8 L2 AND RAF-ERK

=> DUP REM L3
PROCESSING COMPLETED FOR L3
L4            1 DUP REM L3 (7 DUPLICATES REMOVED)

=> D

L4   ANSWER 1 OF 1     MEDLINE                                  DUPLICATE 1
AN   1998244652     MEDLINE
DN   98244652   PubMed ID: 9585253
TI   Activation of tissue-factor gene expression in breast carcinoma cells by
     stimulation of the RAF-ERK signaling pathway.
AU   Zhou J N; Ljungdahl S; Shoshan M C; Swedenborg J; Linder S
CS   Department of Oncology-Pathology, Karolinska Institute and Hospital,
     Stockholm, Sweden.
SO   MOLECULAR CARCINOGENESIS, (1998 Apr) 21 (4) 234-43.
     Journal code: 8811105. ISSN: 0899-1987.
CY   United States
DT   Journal; Article; (JOURNAL ARTICLE)
LA   English
FS   Priority Journals
EM   199805
ED   Entered STN: 19980529
     Last Updated on STN: 20000303
     Entered Medline: 19980520


=> S (CRAF OR RAF-1) AND (1-305 OR 306-648)
   9 FILES SEARCHED...
L5            1 (CRAF OR RAF-1) AND (1-305 OR 306-648)

=> D

L5   ANSWER 1 OF 1  HCAPLUS  COPYRIGHT 2003 ACS
AN   2001:137041  HCAPLUS
DN   134:188193
TI   Protein and cDNA sequences of modified human protein kinase C-Raf and/or
     H-Ras and therapeutic uses thereof for modulation of angiogenesis
IN   Hood, John; Eliceiri, Brian; Cheresh, David A.
PA   The Scripps Research Institute, USA
SO   PCT Int. Appl., 102 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.         KIND  DATE           APPLICATION NO.  DATE
     ---------------    ----  --------       ---------------  --------
PI   WO 2001012210      A1    20010222       WO 2000-US21842  20000811
     WO 2001012210      C2    20020912
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
             HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
             LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
             SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
             YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
             DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,
             CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     EP 1210099         A1    20020605       EP 2000-955423   20000811
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL
     JP 2003507337      T2    20030225       JP 2001-516555   20000811
     NO 2002000718      A     20020410       NO 2002-718      20020212
PRAI US 1999-148924P    P     19990813
     US 2000-215951P    P     20000705
     WO 2000-US21842    W     20000811
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RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS REC
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> S (CRAF OR RAF-1)(5a) kinase domain
9 FILES SEARCHED...
L6 175 (CRAF OR RAF-1)(5A) KINASE DOMAIN

=> dup rem l6
PROCESSING COMPLETED FOR L6
L7 34 DUP REM L6 (141 DUPLICATES REMOVED)

=> d 1-10

L7 ANSWER 1 OF 34 HCAPLUS COPYRIGHT 2003 ACS
AN 2003:83930 HCAPLUS
TI The kinase domain of MEKK1 induces apoptosis by dysregulation of MAP kinase pathways
AU Boldt, Simone; Weidle, Ulrich H.; Kolch, Walter
CS Cancer Research UK, Beatson Institute for Cancer Research, Glasgow, G61 1BD, UK
SO Experimental Cell Research (2003), 283(1), 80-90
CODEN: ECREAL; ISSN: 0014-4827
PB Elsevier Science
DT Journal
LA English
RE.CNT 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 2 OF 34 MEDLINE DUPLICATE 1
AN 2002695410 MEDLINE
DN 22323298 PubMed ID: 12244094
TI Phosphorylation of 338SSYY341 regulates specific interaction between Raf-1 and MEK1.
AU Xiang Xiaoqin; Zang Mengwei; Waelde Christine A; Wen Rong; Luo Zhijun
CS Diabetes and Metabolism Research Unit, Endocrinology Section, Evans Department of Medicine, Boston University School of Medicine, Boston, Massachusetts 02118, USA.
NC GM 57959 (NIGMS)
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (2002 Nov 22) 277 (47) 44996-5003.
Journal code: 2985121R. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200301
ED Entered STN: 20021217
Last Updated on STN: 20030108
Entered Medline: 20030107

L7 ANSWER 3 OF 34 MEDLINE DUPLICATE 2
AN 2000218695 MEDLINE
DN 20218695 PubMed ID: 10753660
TI Association of membrane-associated guanylate kinase-interacting protein-1 with Raf-1.
AU Yao I; Ohtsuka T; Kawabe H; Matsuura Y; Takai Y; Hata Y
CS Department of Medical Biochemistry, Tokyo Medical and Dental University, 1-5-45 Yushima, Bunkyo-ku, Tokyo, 113-8519, Japan.
SO BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (2000 Apr 13) 270 (2) 538-42.
Journal code: 0372516. ISSN: 0006-291X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200005
ED Entered STN: 20000518
Last Updated on STN: 20000518
Entered Medline: 20000508

L7 ANSWER 4 OF 34 MEDLINE DUPLICATE 5
AN 2001223718 MEDLINE
DN 21061396 PubMed ID: 10998357
TI Regulation of the **Raf-1 kinase domain** by phosphorylation and 14-3-3 association.
AU Yip-Schneider M T; Miao W; Lin A; Barnard D S; Tzivion G; Marshall M S
CS Department of Medicine, Indiana University School of Medicine, Indianapolis, IN 46202, USA.
SO BIOCHEMICAL JOURNAL, (2000 Oct 1) 351 (Pt 1) 151-9.
Journal code: 2984726R. ISSN: 0264-6021.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200104
ED Entered STN: 20010502
Last Updated on STN: 20010502
Entered Medline: 20010426

L7 ANSWER 5 OF 34 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT AND ISI
AN 1999-10859 BIOTECHDS
TI Non-human transgenic animal containing oncogenic mutant RAF-1 gene; transgenic animal containing oncogenic Raf gene, used in lung cancer development research
AU Rapp U R
PA Rapp U R
LO Wurzburg, Germany.
PI WO 9928453 10 Jun 1999
AI WO 1998-DE3557 27 Nov 1998
PRAI DE 1997-1054774 28 Nov 1997
DT Patent
LA German
OS WPI: 1999-385380 [32]

L7 ANSWER 6 OF 34 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT AND ISI
AN 1999-05589 BIOTECHDS
TI New isolated human nucleic acid unique to c-raf-1; human c-raf-1 having point mutation in conserved region, may be useful for lung adenocarcinoma susceptibility diagnosis
AU Rapp U R; Storm S M
PA U.S.Dep.Health-Hum.Serv.
LO Washington, DC, USA.
PI US 5869308 9 Feb 1999
AI US 1997-831317 1 Apr 1997
PRAI US 1997-831317 1 Apr 1997
DT Patent
LA English
OS WPI: 1999-152776 [13]

L7 ANSWER 7 OF 34 MEDLINE DUPLICATE 6
AN 1999240702 MEDLINE
DN 99240702 PubMed ID: 10224075
TI Nerve growth factor-stimulated B-Raf catalytic activity is refractory to inhibition by cAMP-dependent protein kinase.
AU MacNicol M C; MacNicol A M
CS Department of Medicine and the Committee on Cancer Biology, The University of Chicago, Chicago, Illinois 60637, USA.
NC CA70846 (NCI)
P60 DK20595-18 (NIDDK)
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1999 May 7) 274 (19) 13193-7.
Journal code: 2985121R. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199906
ED Entered STN: 19990614
Last Updated on STN: 19990614

Entered Medline: 19990603

L7 ANSWER 8 OF 34 SCISEARCH COPYRIGHT 2003 THOMSON ISIDUPLICATE 7
AN 1999:807015 SCISEARCH
GA The Genuine Article (R) Number: 247DX
TI Bacterially expressed Raf-1 catalytic domain is highly associated with GroEL
AU Ho M F (Reprint); Wilson B A; Peterson J W
CS WRIGHT STATE UNIV, SCH MED, DEPT BIOCHEM & MOL BIOL, DAYTON, OH 45435 (Reprint)
CYA USA
SO JOURNAL OF THE CHINESE CHEMICAL SOCIETY, (OCT 1999) Vol. 46, No. 5, pp. 735-742.
Publisher: CHINESE CHEM SOC, PO BOX 609, TAIPEI 10099, TAIWAN.
ISSN: 0009-4536.
DT Article; Journal
FS PHYS
LA English
REC Reference Count: 42
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

L7 ANSWER 9 OF 34 MEDLINE DUPLICATE 8
AN 1998380517 MEDLINE
DN 98380517 PubMed ID: 9712920
TI Activated raf induces the hyperphosphorylation of stathmin and the reorganization of the microtubule network.
AU Lovric J; Dammeier S; Kieser A; Mischak H; Kolch W
CS Institut fur Klinische Molekularbiologie und Tumorgenetik der GSF, Marchioninistrasse 25, D-81377 Munich, Germany.. Lovric@gsf.de
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1998 Aug 28) 273 (35) 22848-55.
Journal code: 2985121R. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199809
ED Entered STN: 19981006
Last Updated on STN: 19981006
Entered Medline: 19980924

L7 ANSWER 10 OF 34 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 1999:57134 BIOSIS
DN PREV199900057134
TI Identification of radicicol as an inhibitor of in vivo Ras/Raf interaction with the yeast two-hybrid screening system.
AU Ki, Se Won; Kasahara, Koji; Kwon, Ho Jeong; Eishima, Jun; Takesako, Kazutoh; Cooper, Jonathan A.; Yoshida, Minoru (1); Horinouchi, Sueharu
CS (1) Dep. Biotechnol., Grad. Sch. Agric. Life Sci., Univ. Tokyo, Bunkyo-ku, Tokyo 113 Japan
SO Journal of Antibiotics (Tokyo), (Oct., 1998) Vol. 51, No. 10, pp. 936-944.
ISSN: 0021-8820.
DT Article
LA English

=> d 2-8 kwic

L7 ANSWER 2 OF 34 MEDLINE DUPLICATE 1
AB The present study characterizes the interaction between the **Raf-1 kinase domain** and MEK1 and examines whether the magnitude of their interaction correlates to the ability of Raf to phosphorylate MEK1. Here. . .

L7 ANSWER 3 OF 34 MEDLINE DUPLICATE 2
AB . . . have tested whether MAGUIN-1 interacts directly with Raf-1. MAGUIN-1 and Raf-1 were coimmunoprecipitated from rat brain. MAGUIN-1 binds to the **kinase domain** of **Raf-1** , and **Raf-1** binds to the middle region of MAGUIN-1 containing the PH domain. However, in contrast to the dominant active

mutant of. . .

L7 ANSWER 4 OF 34 MEDLINE DUPLICATE 3
TI Regulation of the **Raf-1 kinase domain** by phosphorylation and 14-3-3 association.
AB The **Raf-1 kinase domain** is kept in an inactive state by the N-terminal regulatory domain. Activation of the kinase domain occurs following release from. . .

L7 ANSWER 5 OF 34 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT AND ISI
AB. . . c-Raf-1 gene, is claimed. Also claimed is a non-human transgenic mammal containing foreign DNA with a constitutively active oncogenic mutant **kinase-domain** of the c-**Raf-1** gene, or an equivalent normal allele or derivative of A, B or c-Raf-1. The claims also cover a process for. . .

L7 ANSWER 6 OF 34 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT AND ISI
AB. . . c-raf-1 gene is claimed. No uses are stated, but the presence of point mutations in the conserved region (CR3, the **kinase domain**) of c-**raf-1** is indicative of an increased risk of developing cancer (particularly lung adenocarcinoma) and is useful for deriving appropriate therapeutic strategies.. . .

L7 ANSWER 7 OF 34 MEDLINE DUPLICATE 6
AB . . . inhibition, of PC12 cell differentiation is curious in light of the ability of PKA to inhibit Raf-1 catalytic activity. The **kinase domains** of **Raf-1** and B-Raf are highly conserved, and it has been predicted that B-Raf catalytic activity would also be inhibited by PKA.. . .

L7 ANSWER 8 OF 34 SCISEARCH COPYRIGHT 2003 THOMSON ISIDUPLICATE 7
AB . . . Binding of GroEL and ELISA analysis revealed a preferential GroEL binding site in the beta 1 sheet region of the **Raf-1 kinase domain**.

=> d 2-8 ab

L7 ANSWER 2 OF 34 MEDLINE DUPLICATE 1
AB The present study characterizes the interaction between the **Raf-1 kinase domain** and MEK1 and examines whether the magnitude of their interaction correlates to the ability of Raf to phosphorylate MEK1. Here we show that the minimal domain required for the Raf kinase activity starts from tryptophan 342. Maximal binding of the Raf kinase domain to MEK1 and its kinase activity are achieved upon phosphorylation of the region (338)SSYY(341) in response to 4beta-12-O-tetradecanoylphorbol-13-acetate (TPA), or mutation of Y340Y341 to aspartic acids. Conversely, the TPA-stimulated MEK binding and kinase activity are diminished when this region is deleted or Ser(338) and Ser(339) are mutated to alanines. We also show that the integrity of the Raf ATP-binding site is necessary for the interaction between Raf-1 and MEK1. Furthermore, two MEK-binding sites are identified; the first is localized between amino acids 325 and 349, and the second is within the region between amino acids 350 and 648. Separately, the binding of each site to MEK1 is weak, but in a cis context, they give rise to a much stronger association, which can be further stimulated by TPA. Finally, we find that tryptophan 342, which is conserved among the Raf family and other protein kinases, is essential for the Ser(338) phosphorylation of the full-length Raf and its binding to MEK1. Taken together, our results indicate that the phosphorylation of Ser(338) and Tyr(341) on Raf exerts an important effect on reconfiguring the two MEK-binding sites. As a result, these two sites coordinate to form a high affinity MEK-binding epitope, leading to a marked increase in Raf kinase activity.

L7 ANSWER 3 OF 34 MEDLINE DUPLICATE 2
AB Membrane-associated guanylate kinase-interacting protein (MAGUIN)-1 was identified as a protein interacting with synaptic scaffolding molecule (S-SCAM) and postsynaptic density (PSD)-95/synapse-associated protein (SAP)90. MAGUIN-1 has a chimerical molecular structure composed of one

sterile alpha motif, one PS[redacted]95/Dlg-A/ZO-1 (PDZ), and one pl[redacted]strin homology (PH) domain, and interacts with the PDZ domains of S-SCAM and PSD-95/SAP90 via its carboxyl-terminal PDZ-binding motif. MAGUIN-1 is considered as a mammalian homologue of Drosophila CNK, which is a Raf-interacting protein implicated in the regulation of eye development. Here we have tested whether MAGUIN-1 interacts directly with Raf-1. MAGUIN-1 and Raf-1 were coimmunoprecipitated from rat brain. MAGUIN-1 binds to the **kinase domain** of **Raf-1**
, and **Raf-1** binds to the middle region of MAGUIN-1
containing the PH domain. However, in contrast to the dominant active mutant of Ki-Ras, which interacts with Raf-1, recruits it to the plasma membrane from the cytosol, and activates it, MAGUIN-1 neither activates Raf-1 nor recruits it to the plasma membrane. MAGUIN-1 may link Raf-1 to components of synapses assembled by PSD-95/SAP90 and S-SCAM.

L7 ANSWER 4 OF 34 MEDLINE DUPLICATE 3
AB The **Raf-1 kinase domain** is kept in
an inactive state by the N-terminal regulatory domain. Activation of the kinase domain occurs following release from the N-terminal repression and possible catalytic upregulation. To distinguish the regulatory mechanisms that directly influence the catalytic activity of the enzyme from those which act through the inhibitory domain, the catalytic domain of Raf-1 (CR3) was expressed in COS-7 cells. The role of phosphorylation in the direct regulation of this domain was determined by substituting non-phosphorylatable amino acids for known serine and tyrosine phosphorylation sites. The intrinsic activity of each mutant protein was determined as well as stimulation by v-Src and phorbol esters. Both v-Src and phorbol esters were potent activators of CR3, requiring the serine 338/339 (p21-activated protein kinase, Pak) and tyrosine 340/341 (Src) phosphorylation sites for full stimulation of CR3. In contrast, loss of the serine 497/499 protein kinase C phosphorylation sites had little effect on CR3 activation by either v-Src or phorbol esters. Loss of serine 621, a 14-3-3 adaptor-protein-binding site, prevented activation of CR3 by v-Src or phorbol esters and partially decreased the high basal activity of the kinase fragment. When co-expressed in COS-7 cells, 14-3-3 associated strongly with full-length Raf-1, weakly with wild-type CR3 and not at all with the A621 and D621 CR3 mutants. The role of 14-3-3 in maintaining the activity of the catalytic domain of Raf-1 was investigated further by performing peptide-competition studies with wild-type CR3, wild-type CR3 and v-Src or constitutively active CR3 (CR3[YY340/341DD]). In each case, incubation of the proteins with a phosphoserine-621 Raf-1 peptide, which we show displaced Raf-1 and CR3[YY340/341DD] from 14-3-3, was found to substantially reduce catalytic activity. Taken together, our results support a model of Raf regulation in which the activity of the Raf-1 catalytic domain is directly upregulated by phosphorylation, following relief of inhibition by the N-terminal regulatory domain upon Ras-GTP binding. Moreover, the presence of serine 621 in the free catalytic fragment is required for full CR3 activation by stimulatory factors, and the continuous presence of 14-3-3 at this site is necessary for retaining activity once the kinase is activated.

L7 ANSWER 5 OF 34 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT AND ISI
AB A non-human transgenic animal with cells that express a constitutively active c-Raf-1 gene with an oncogenic mutation in the kinase-domain, or a protein encoded by a corresponding normal allele or derivative of the A, B or c-Raf-1 gene, is claimed. Also claimed is a non-human transgenic mammal containing foreign DNA with a constitutively active oncogenic mutant **kinase-domain** of the c-**Raf-1**
gene, or an equivalent normal allele or derivative of A, B or c-Raf-1. The claims also cover a process for production of that transgenic animal, and a tissue sample, particularly of lung tissue, derived from the transgenic animal, characterized by an increased tendency to form tumors. Also covered is a means of producing that tissue sample from the transgenic animal, and a recombinant vector containing a DNA sequence that encodes the mutant kinase-domain, a surfactant-C-protein promoter, and optionally SV40 virus DNA. The vector is used to produce the transgenic animal, and tissues derived from that animal. The transgenic tissues are used in research into the development of lung cancer,

particularly lung carcinom (42pp)

L7 ANSWER 6 OF 34 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT AND ISI
AB A novel isolated DNA sequence (I) having a point mutation in the conserved region encoding amino acids 450-630 of the 630 protein sequence encoding the human c-raf-1 gene is claimed. No uses are stated, but the presence of point mutations in the conserved region (CR3, the **kinase domain**) of c-**raf-1** is indicative of an increased risk of developing cancer (particularly lung adenocarcinoma) and is useful for deriving appropriate therapeutic strategies. (26pp)

L7 ANSWER 7 OF 34 MEDLINE DUPLICATE 6
AB The cAMP-dependent protein kinase (PKA) exhibits both inhibitory and stimulatory effects upon growth factor signaling mediated by the mitogen-activated protein kinase signaling pathway. PKA has been demonstrated to inhibit Raf-1-mediated cellular proliferation. PKA can both prevent Ras-dependent Raf-1 activation and directly inhibit Raf-1 catalytic activity. In contrast to the inhibitory effect of PKA on Raf-1-dependent processes, PKA potentiates nerve growth factor-stimulated PC12 cell differentiation, a B-Raf mediated process. This potentiation, rather than inhibition, of PC12 cell differentiation is curious in light of the ability of PKA to inhibit Raf-1 catalytic activity. The **kinase domains** of **Raf-1** and B-Raf are highly conserved, and it has been predicted that B-Raf catalytic activity would also be inhibited by PKA. In this study we examined the ability of PKA to regulate the kinase activity of the B-raf proto-oncogene. We report that nerve growth factor-stimulated B-Raf activity is not inhibited by PKA. By contrast, an N-terminally truncated, constitutively active form of B-Raf is inhibited by PKA both in vitro and in transfected PC12 cells. These results suggest that the N-terminal regulatory domain interferes with the ability of PKA to modulate B-Raf catalytic activity and provide an explanation for the observed resistance of B-Raf-dependent processes to PKA inhibition.

L7 ANSWER 8 OF 34 SCISEARCH COPYRIGHT 2003 THOMSON ISIDUPLICATE 7
AB Raf-1 is a key protein kinase in the mitogen-activated protein kinase cascade. We have subcloned the catalytic domain of Raf-1 into the bacterial expression vectors, pTrcHisB and pGEX-6P-1, denoted as His(6)-Delta Raf and GST-RafBXB, respectively. Chromatography of the recombinant proteins using Ni-NTA agarose, Sephacryl S-300, and glutathione-sepharose revealed association of Raf-1 catalytic domain in a high molecular weight complex with a 57 kDa protein. Microsequencing of this 57 kDa protein identified it as GroEL, a heat shock protein in E. coli important far protein folding. GroEL association with the Raf-1 catalytic domain is specific, as evidenced by its association with both Raf-1 constructs. Native-PAGE gels and Western analysis of gel filtration fractions revealed association of the catalytic domain with a large molecular weight complex consistent with the tetradecameric complex of GroEL. A peptide library of 384 dodecapeptides corresponding to the entire catalytic domain of Raf-1 was constructed by the spot synthesis method. Binding of GroEL and ELISA analysis revealed a preferential GroEL binding site in the beta 1 sheet region of the **Raf-1** **kinase domain**.

=> d 11-20

L7 ANSWER 11 OF 34 MEDLINE DUPLICATE 9
AN 1998124186 MEDLINE
DN 98124186 PubMed ID: 9464539
TI Regulation of c-myc expression by Ras/Raf signalling.
AU Kerkhoff E; Houben R; Loffler S; Troppmair J; Lee J E; Rapp U R
CS Institut fur medizinische Strahlenkunde und Zellforschung, University of Wurzburg, Germany.
SO ONCOGENE, (1998 Jan 15) 16 (2) 211-6.
Journal code: 8711562. ISSN: 0950-9232.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)

LA English
FS Priority Journals
EM 199802
ED Entered STN: 19980226
Last Updated on STN: 20000303
Entered Medline: 19980219

L7 ANSWER 12 OF 34 MEDLINE DUPLICATE 10
AN 1998077317 MEDLINE
DN 98077317 PubMed ID: 9416835
TI Protein kinase C-epsilon associates with the Raf-1 kinase and induces the production of growth factors that stimulate Raf-1 activity.
AU Ueffing M; Lovric J; Philipp A; Mischak H; Kolch W
CS GSF-Forschungszentrum fur Umwelt und Gesundheit, Instit fur Klinische Molekularbiologie und Tumorgenetik, Munchen.
SO ONCOGENE, (1997 Dec 11) 15 (24) 2921-7.
Journal code: 8711562. ISSN: 0950-9232.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199801
ED Entered STN: 19980129
Last Updated on STN: 19980129
Entered Medline: 19980115

L7 ANSWER 13 OF 34 MEDLINE DUPLICATE 11
AN 97299872 MEDLINE
DN 97299872 PubMed ID: 9155021
TI Mammalian Raf-1 is activated by mutations that restore Raf signaling in Drosophila.
AU Cutler R E Jr; Morrison D K
CS Molecular Basis of Carcinogenesis Laboratory, ABL-Basic Research Program, National Cancer Institute, Frederick Cancer Research and Development Center, MD 21702, USA.
SO EMBO JOURNAL, (1997 Apr 15) 16 (8) 1953-60.
Journal code: 8208664. ISSN: 0261-4189.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199706
ED Entered STN: 19970716
Last Updated on STN: 20000303
Entered Medline: 19970627

L7 ANSWER 14 OF 34 MEDLINE DUPLICATE 12
AN 97429918 MEDLINE
DN 97429918 PubMed ID: 9285556
TI Mutations of critical amino acids affect the biological and biochemical properties of oncogenic A-Raf and Raf-1.
AU Bosch E; Cherwinski H; Peterson D; McMahon M
CS Department of Cell Signaling, DNAX Research Institute, Palo Alto, California 94304-1104, USA.
SO ONCOGENE, (1997 Aug 28) 15 (9) 1021-33.
Journal code: 8711562. ISSN: 0950-9232.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199709
ED Entered STN: 19971008
Last Updated on STN: 20000303
Entered Medline: 19970922

L7 ANSWER 15 OF 34 MEDLINE DUPLICATE 13
AN 1998053492 MEDLINE
DN 98053492 PubMed ID: 9392004
TI Constitutive modulation of Raf-1 protein kinase is associated with

differential gene expressi[redacted]of several known and unknown g[redacted]s.
AU Patel S; Wang F H; Whiteside T L; Kasid U
CS Department of Radiation Medicine, Lombardi Cancer Center, Georgetown University, Washington, D.C. 20007, USA.
NC CA58984 (NCI)
CA68322 (NCI)
OD68322 (NIH)
+
SO MOLECULAR MEDICINE, (1997 Oct) 3 (10) 674-85.
Journal code: 9501023. ISSN: 1076-1551.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-U70771; GENBANK-U70772
EM 199801
ED Entered STN: 19980217
Last Updated on STN: 19980217
Entered Medline: 19980130

L7 ANSWER 16 OF 34 MEDLINE DUPLICATE 14
AN 97175147 MEDLINE
DN 97175147 PubMed ID: 9022807
TI Correlation of constitutive activation of raf-1 with morphological transformation and abrogation of tyrosine phosphorylation of distinct sets of proteins in human squamous carcinoma cells.
AU Patel B K; Ray S; Whiteside T L; Kasid U
CS Department of Radiation Medicine, Lombardi Cancer Center, Georgetown University Medical Center, Washington, DC 20007, USA.
NC CA58954 (NCI)
CA68322 (NCI)
SO MOLECULAR CARCINOGENESIS, (1997 Jan) 18 (1) 1-6.
Journal code: 8811105. ISSN: 0899-1987.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199702
ED Entered STN: 19970306
Last Updated on STN: 19980206
Entered Medline: 19970227

L7 ANSWER 17 OF 34 MEDLINE DUPLICATE 15
AN 96413291 MEDLINE
DN 96413291 PubMed ID: 8816453
TI Negative regulation of Raf-1 by phosphorylation of serine 621.
AU Mischak H; Seitz T; Janosch P; Eulitz M; Steen H; Schellerer M; Philipp A; Kolch W
CS GSF-Institut fur Klinische Molekularbiologie und Tumorgenetik, Munich, Germany.
SO MOLECULAR AND CELLULAR BIOLOGY, (1996 Oct) 16 (10) 5409-18.
Journal code: 8109087. ISSN: 0270-7306.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199611
ED Entered STN: 19961219
Last Updated on STN: 20000303
Entered Medline: 19961115

L7 ANSWER 18 OF 34 MEDLINE DUPLICATE 16
AN 96275763 MEDLINE
DN 96275763 PubMed ID: 8665528
TI Suppression of a human colon cancer cell line by introduction of an exogenous NF1 gene.
AU Li Y; White R
CS Howard Hughes Medical Institute, University of Utah, Salt Lake City, Utah 84112, USA.

SO CANCER RESEARCH, (1996 Jun [redacted] 56 (12) 2872-6.
Journal code: 2984705R. ISSN: 0008-5472.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199608
ED Entered STN: 19960819
Last Updated on STN: 20000303
Entered Medline: 19960806

L7 ANSWER 19 OF 34 MEDLINE DUPLICATE 17
AN 96404523 MEDLINE
DN 96404523 PubMed ID: 8808705
TI Inhibition of Raf-1 signaling by a monoclonal antibody, which interferes with Raf-1 activation and with Mek substrate binding.
AU Kolch W; Philipp A; Mischak H; Dutil E M; Mullen T M; Feramisco J R; Meinkoth J L; Rose D W
CS Department of Medicine, University of California at San Diego, La Jolla 92093, USA.
SO ONCOGENE, (1996 Sep 19) 13 (6) 1305-14.
Journal code: 8711562. ISSN: 0950-9232.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199611
ED Entered STN: 19961219
Last Updated on STN: 20020420
Entered Medline: 19961108

L7 ANSWER 20 OF 34 MEDLINE DUPLICATE 18
AN 95294017 MEDLINE
DN 95294017 PubMed ID: 7539798
TI Functional mapping of the N-terminal regulatory domain in the human Raf-1 protein kinase.
AU Chow Y H; Pumiglia K; Jun T H; Dent P; Sturgill T W; Jove R
CS Department of Microbiology and Immunology, University of Michigan Medical School, Ann Arbor 48109, USA.
NC CA55652 (NCI)
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1995 Jun 9) 270 (23) 14100-6.
Journal code: 2985121R. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199507
ED Entered STN: 19950720
Last Updated on STN: 20000303
Entered Medline: 19950710

=> d 14, 20

L7 ANSWER 14 OF 34 MEDLINE DUPLICATE 12
AN 97429918 MEDLINE
DN 97429918 PubMed ID: 9285556
TI Mutations of critical amino acids affect the biological and biochemical properties of oncogenic A-Raf and Raf-1.
AU Bosch E; Cherwinski H; Peterson D; McMahon M
CS Department of Cell Signaling, DNAX Research Institute, Palo Alto, California 94304-1104, USA.
SO ONCOGENE, (1997 Aug 28) 15 (9) 1021-33.
Journal code: 8711562. ISSN: 0950-9232.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199709

ED Entered STN: 19971008
Last Updated on STN: 20000303
Entered Medline: 19970922

L7 ANSWER 20 OF 34 MEDLINE DUPLICATE 18
AN 95294017 MEDLINE
DN 95294017 PubMed ID: 7539798
TI Functional mapping of the N-terminal regulatory domain in the human Raf-1 protein kinase.
AU Chow Y H; Pumiglia K; Jun T H; Dent P; Sturgill T W; Jove R
CS Department of Microbiology and Immunology, University of Michigan Medical School, Ann Arbor 48109, USA.
NC CA55652 (NCI)
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1995 Jun 9) 270 (23) 14100-6.
Journal code: 2985121R. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199507
ED Entered STN: 19950720
Last Updated on STN: 20000303
Entered Medline: 19950710

=> d 14, 20 ab

L7 ANSWER 14 OF 34 MEDLINE DUPLICATE 12
AB The catalytic domains of the Raf family of protein kinases (deltaRaf) differ in their ability to activate MEK in vitro and in vivo and in their ability to oncogenically transform mammalian cells. The kinase domain of B-Raf is more active than the equivalent portion of Raf-1 which in turn is more active than A-Raf. In Raf-1 the phosphorylation or mutation to aspartic acid of two key tyrosine residues upstream of the ATP binding site has been demonstrated to significantly potentiate catalytic activity. In A-Raf the analogous amino acids are also tyrosine whereas in B-Raf they are aspartic acid. To determine if these differences in amino acid sequence influence the relative catalytic activity of the Raf kinase domains we constructed forms of deltaA-Raf, deltaB-Raf and deltaRaf-1 that encode either aspartic acid [DD], phenylalanine [FF] or tyrosine [YY] at these positions. These proteins were expressed both in mammalian cells as fusions with the hormone binding domain of the estrogen receptor and as epitope-tagged proteins in Sf9 insect cells to test their oncogenic and catalytic potentials. When expressed in Rat1 or 3T3 cells in the presence of hormone all of the deltaRaf-1:ER and deltaA-Raf:ER proteins were transforming with the exception of the [FF] form of deltaA-Raf. In general the [DD] forms of the deltaRaf-1:ER and deltaA-Raf:ER proteins were the most potently oncogenic which correlated with their ability to elicit activation of the MAP kinase pathway. Consistent with the transformation data, the catalytic activity of the [DD] forms of deltaA-Raf:ER and deltaRaf-1:ER was about ten times greater than the cognate [FF] and [YY] forms of the proteins. By contrast all of the deltaB-Raf:ER proteins were highly transforming and deltaB-Raf catalytic activity was largely unaffected by mutation of the aforementioned aspartic acids to either tyrosine or phenylalanine. Similar results were obtained with epitope-tagged forms of deltaA-Raf, deltaB-Raf and deltaRaf-1 expressed in Sf9 cells. These data provide support for the model that key tyrosine residues in the protein **kinase domains** of A-Raf and **Raf-1** are important in the regulation of catalytic activity. In addition they demonstrate that the higher intrinsic activity of B-Raf cannot be explained simply by the presence of aspartic acids at the analogous positions.

L7 ANSWER 20 OF 34 MEDLINE DUPLICATE 18
AB Raf-1 is a serine/threonine kinase poised at a key relay point in mitogenic signal transduction pathways from the cell surface to the nucleus. Activation of the transforming potential of Raf-1 has been associated with N-terminal truncation and/or fusion to other proteins, suggesting that the Raf-1 N-terminal half harbors a negative regulatory

domain. Seven internal deletion mutants that together scan the entire N-terminal half of human Raf-1 protein were generated to map functional regions in this regulatory domain. Effects of the deletion mutations on kinase activity of Raf-1 were evaluated using a baculovirus/insect cell overexpression system and an in vitro kinase assay with the known physiological substrate of Raf-1, mitogen-activated protein kinase kinase. Deletion of amino acids 276-323 in the unique sequence between conserved regions 2 and 3 leads to modest elevation of Raf-1 basal kinase activity, whereas deletion of amino acids 133-180 in conserved region 1 results in diminished kinase activity. Surprisingly, none of the Raf-1 N-terminal deletion mutants, including a truncated version that is transforming in rodent fibroblasts, exhibits greatly increased levels of basal kinase activity. In addition, while activation of Raf-1 kinase by Ras requires sequences in conserved region 1, only the C-terminal half containing the **kinase domain** of **Raf-1** is required
for activation by Src. These findings demonstrate that N-terminal deletions in Raf-1 do not necessarily result in constitutively elevated basal kinase activity and that the N-terminal regulatory domain is completely dispensable for Raf-1 activation by Src.

=> d 21-30

L7 ANSWER 21 OF 34 MEDLINE DUPLICATE 19
AN 96030784 MEDLINE
DN 96030784 PubMed ID: 7588608
TI ERF: an ETS domain protein with strong transcriptional repressor activity, can suppress ets-associated tumorigenesis and is regulated by phosphorylation during cell cycle and mitogenic stimulation.
AU Sgouras D N; Athanasiou M A; Beal G J Jr; Fisher R J; Blair D G; Mavrothalassitis G J
CS Laboratory of Molecular Oncology, National Cancer Institute, Frederick, MD 21702-1201, USA.
SO EMBO JOURNAL, (1995 Oct 2) 14 (19) 4781-93.
Journal code: 8208664. ISSN: 0261-4189.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-U15655
EM 199511
ED Entered STN: 19960124
Last Updated on STN: 20000303
Entered Medline: 19951128

L7 ANSWER 22 OF 34 MEDLINE DUPLICATE 20
AN 95188873 MEDLINE
DN 95188873 PubMed ID: 7882972
TI Regulation of Raf-1 kinase activity by the 14-3-3 family of proteins.
AU Li S; Janosch P; Tanji M; Rosenfeld G C; Waymire J C; Mischak H; Kolch W; Sedivy J M
CS Department of Molecular Biophysics and Biochemistry, Yale University School of Medicine, New Haven, CT 06520.
NC GM-R01-41690 (NIGMS)
SO EMBO JOURNAL, (1995 Feb 15) 14 (4) 685-96.
Journal code: 8208664. ISSN: 0261-4189.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199504
ED Entered STN: 19950425
Last Updated on STN: 19980206
Entered Medline: 19950407

L7 ANSWER 23 OF 34 MEDLINE DUPLICATE 21
AN 95408256 MEDLINE
DN 95408256 PubMed ID: 7545901
TI The 33-kDa C-terminal domain of Raf-1 protein kinase exhibits a

Ras-independent serum- and [redacted]orbol ester-induced shift in g[redacted]obility.
AU Olah Z; Ferrier A; Lehel C; Anderson W B
CS Laboratory of Cellular Oncology, National Cancer Institute, National Institutes of Health, Bethesda, MD 20892, USA.
SO BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (1995 Sep 14) 214 (2) 340-7.
Journal code: 0372516. ISSN: 0006-291X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199510
ED Entered STN: 19951026
Last Updated on STN: 20000303
Entered Medline: 19951019

L7 ANSWER 24 OF 34 MEDLINE DUPLICATE 22
AN 95021198 MEDLINE
DN 95021198 PubMed ID: 7935389
TI Mechanism of inhibition of Raf-1 by protein kinase A.
AU Hafner S; Adler H S; Mischak H; Janosch P; Heidecker G; Wolfman A; Pippig S; Lohse M; Ueffing M; Kolch W
CS Institut fur Klinische Molekularbiologie und Tumorgenetik, Munich.
SO MOLECULAR AND CELLULAR BIOLOGY, (1994 Oct) 14 (10) 6696-703.
Journal code: 8109087. ISSN: 0270-7306.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199410
ED Entered STN: 19941222
Last Updated on STN: 20020420
Entered Medline: 19941021

L7 ANSWER 25 OF 34 MEDLINE DUPLICATE 23
AN 94289818 MEDLINE
DN 94289818 PubMed ID: 8019003
TI Raf-1 interferes with Ras and Rap1A effector functions in yeast.
AU Ruggieri R; Macdonald S G; Callow M; McCormick F
CS Onyx Pharmaceuticals, Richmond, California.
NC CA60443 (NCI)
NCI: CA51992-04 (NCI)
SO MOLECULAR BIOLOGY OF THE CELL, (1994 Feb) 5 (2) 173-81.
Journal code: 9201390. ISSN: 1059-1524.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199408
ED Entered STN: 19940815
Last Updated on STN: 20000303
Entered Medline: 19940802

L7 ANSWER 26 OF 34 HCAPLUS COPYRIGHT 2003 ACS
AN 1993:492494 HCAPLUS
DN 119:92494
TI Oncogene activation: c-raf-1 gene mutations in experimental and naturally occurring tumors
AU Storm, Stephen M.; Rapp, Ulf R.
CS Frederick Cancer Res. Dev. Cent., Frederick, MD, USA
SO Toxicology Letters (1993), 67(1-3), 201-10
CODEN: TOLED5; ISSN: 0378-4274
DT Journal; General Review
LA English

L7 ANSWER 27 OF 34 HCAPLUS COPYRIGHT 2003 ACS
AN 1991:226728 HCAPLUS
DN 114:226728
TI The Raf-1 kinase as a transducer of mitogenic signals

AU Morrison, Deborah K.
CS Frederick Cancer Res. Dev. Cent., NCI, Frederick, MD, 21702, USA
SO Cancer Cells (1989) (1990), 2(12), 377-82
CODEN: CCELER; ISSN: 1042-2196
DT Journal; General Review
LA English

L7 ANSWER 28 OF 34 MEDLINE DUPLICATE 24
AN 89239469 MEDLINE
DN 89239469 PubMed ID: 2524024
TI A mechanism of c-raf-1 activation: fusion of the lipocortin II amino-terminal sequence with the c-**raf-1** **kinase domain**.
AU Mitsunobu F; Fukui M; Oda T; Yamamoto T; Toyoshima K
CS The Institute of Medical Science, University of Tokyo, Japan.
SO ONCOGENE, (1989 Apr) 4 (4) 437-42.
Journal code: 8711562. ISSN: 0950-9232.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198906
ED Entered STN: 19900306
Last Updated on STN: 19980206
Entered Medline: 19890612

L7 ANSWER 29 OF 34 SCISEARCH COPYRIGHT 2003 THOMSON ISI
AN 89:266798 SCISEARCH
GA The Genuine Article (R) Number: U5677
TI A MECHANISM OF C-RAF-1 ACTIVATION - FUSION OF THE LIPOCORTIN-II AMINO-TERMINAL SEQUENCE WITH THE C-**RAF-1** **KINASE DOMAIN**
AU MITSUNOBU F; FUKUI M; ODA T; YAMAMOTO T (Reprint); TOYOSHIMA K
CS UNIV TOKYO, INST MED SCI, 4-6-1 SHIROKANEDAI, MINATO KU, TOKYO 108, JAPAN; OKAYAMA UNIV, SCH MED, OKAYAMA 700, JAPAN
CYA JAPAN
SO ONCOGENE, (1989) Vol. 4, No. 4, pp. 437-442.
DT Article; Journal
FS LIFE
LA ENGLISH
REC Reference Count: 39

L7 ANSWER 30 OF 34 MEDLINE DUPLICATE 25
AN 87269680 MEDLINE
DN 87269680 PubMed ID: 3300556
TI Activated c-raf-1 gene from human stomach cancer.
AU Shimizu K; Nakatsu Y; Oh-uchida M; Nomoto S; Sekiguchi M
SO GAN TO KAGAKU RYOHO [JAPANESE JOURNAL OF CANCER AND CHEMOTHERAPY], (1987 Jun) 14 (6 Pt 2) 2140-6.
Journal code: 7810034. ISSN: 0385-0684.
CY Japan
DT Journal; Article; (JOURNAL ARTICLE)
LA Japanese
FS Priority Journals
EM 198707
ED Entered STN: 19900305
Last Updated on STN: 19900305
Entered Medline: 19870727

=> d 23, 26, 28, 29 ab

L7 ANSWER 23 OF 34 MEDLINE DUPLICATE 21
AB Experiments were carried out to determine **Raf-1** protein **kinase domain** fragments which exhibit a characteristic electrophoretic mobility shift noted with Raf-1 protein kinase in response to serum and phorbol ester (PMA) treatment of serum-deprived NIH 3T3 cells. Epsilon-epitope tagged 84 kDa Raf-1 holoenzyme (HR-epsilon), as well as the epsilon-epsilon pitope tagged 35

kDa N-terminal (RI-epsilon) 33 kDa mid-portion (RII-epsilon) and 33 kDa C-terminal (RIII-epsilon) fragments of Raf-1 were overexpressed in NIH 3T3 cells. The overexpressed HR-epsilon exhibited a serum- and PMA-induced shift in gel mobility similar to that noted with endogenous Raf-1. The C-terminal RIII-epsilon fragment exhibited a similar shift in gel mobility while the electrophoretic mobility of the N-terminal RI-epsilon fragment remained unchanged. These results suggest that modification(s) within the 33 kDa C-terminal portion of Raf-1 which occur independently of association with Ras may be responsible for the band shift observed with serum and PMA treatment of serum-deprived NIH 3T3 cells.

L7 ANSWER 26 OF 34 HCAPLUS COPYRIGHT 2003 ACS
AB The authors demonstrate here consistent point mutations of the c-raf-1 proto-oncogene, within a small region of the kinase domain, in a mouse model for chem. tumor induction. This is the 1st demonstration of point mutated raf genes in vivo, and the 1st isolation of activating, in vivo point mutations in the kinase domain of a proto-oncogene. The specific region where these mutations are clustered also has biol. significance. This is precisely the region where 5/5 independently generated monoclonal antibodies raised against Raf-1 map to, and predictions based upon the crystal structure of A kinase identify this as the substrate pocket. The tumors examd. show a selective specificity for Raf-1 mutations in that another family of genes, the ras proto-oncogenes which are frequently activated by point mutation in both animal and human tumors, is NOT: general involved. The authors consistent finding of Raf-1 mutations in a mouse tumor model also has consequences for further evaluation of the role of Raf-1 in human tumor development, as it emphasizes the need to examine c-raf-1 at the sequence level. In fact preliminary screening of human lung tumors indicates point mutations at amino acid 533. Finally, the cumulative data on the crit. role of Raf-1 in signal transduction and the occurrence of oncogenic Raf-1 in tumors highlight this enzyme as an attractive target for development of novel anticancer regimens.

L7 ANSWER 28 OF 34 MEDLINE DUPLICATE 24
AB In order to understand the mechanism of oncogenic activation, we have analyzed the c-raf-1 gene from the GL-5-JCK human glioblastoma, which underwent rearrangement during transfection experiments. Nucleotide sequencing of cDNA clones derived from the 2.5 kb raf-mRNA, which is a major transcript of raf in NIH3T3 cells transformed with GL-5-JCK DNA, revealed that this mRNA contains sequences derived from the human c-raf-1 gene and the human lipocortin II gene. Translation of the 2.5 kb raf-mRNA predicted a fusion protein consisting of 16 amino-terminal amino acid residues of the lipocortin II and 370 carboxy-terminal amino acid residues of the c-**raf-1** protein which contains the **kinase domain**. Expression of the lipocortin II-raf cDNA using the murine sarcoma virus long terminal repeat as promoter resulted in the transformation of NIH3T3 cells.

L7 ANSWER 29 OF 34 SCISEARCH COPYRIGHT 2003 THOMSON ISI

=> d 31-34

L7 ANSWER 31 OF 34 MEDLINE DUPLICATE 26
AN 87292133 MEDLINE
DN 87292133 PubMed ID: 3616625
TI The raf oncogene is associated with a radiation-resistant human laryngeal cancer.
AU Kasid U; Pfeifer A; Weichselbaum R R; Dritschilo A; Mark G E
NC CA425969 (NCI)
SO SCIENCE, (1987 Aug 28) 237 (4818) 1039-41.
Journal code: 0404511. ISSN: 0036-8075.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198709
ED Entered STN: 19900305
Last Updated on STN: 19970203

Entered Medline: 19870924

L7 ANSWER 32 OF 34 LIFESCI COPYRIGHT 2003 CSA
AN 87:50488 LIFESCI
TI The raf oncogene is associated with a radiation-resistant human laryngeal cancer.
AU Kasid, U.; Pfeifer, A.; Weichselbaum, R.R.; Dritschilo, A.; Mark, G.E.
CS Dep. Radiat. Med., Georgetown Univ. Sch. Med., Vincent T. Lombardi Cancer Cent., Washington, DC 20007, USA
SO SCIENCE (WASH.)., (1987) vol. 238, no. 4818, pp. 1039-1040.
DT Journal
FS N; G
LA English
SL English

L7 ANSWER 33 OF 34 HCAPLUS COPYRIGHT 2003 ACS
AN 1988:487252 HCAPLUS
DN 109:87252
TI Structure of the activated c-raf-1 gene from human stomach cancer
AU Shimizu, Kenji; Nakatsu, Yoshimichi; Nomoto, Satoshi; Sekiguchi, Mutsuo
CS Fac. Sci., Kyushu Univ., Fukuoka, 812, Japan
SO Proceedings of the International Symposium of the Princess Takamatsu Cancer Research Fund (1987), Volume Date 1986, 17th(Oncog. Cancer), 85-91
CODEN: PPTCBY
DT Journal
LA English

L7 ANSWER 34 OF 34 MEDLINE
AN 88330725 MEDLINE
DN 88330725 PubMed ID: 2843497
TI Structure of the activated c-raf-1 gene from human stomach cancer.
AU Shimizu K; Nakatsu Y; Nomoto S; Sekiguchi M
CS Molecular Genetics Section, Faculty of Science, Kyushu University, Fukuoka, Japan.
SO PRINCESS TAKAMATSU SYMPOSIA, (1986) 17 85-91.
Journal code: 9301172.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198810
ED Entered STN: 19900308
Last Updated on STN: 19900308
Entered Medline: 19881027

=> d 33, 34 ab

L7 ANSWER 33 OF 34 HCAPLUS COPYRIGHT 2003 ACS
AB A novel human transforming gene was previously isolated from a primary stomach cancer and was identified as an activated version of the c-raf-1 gene which is the human homolog of v-raf, a viral oncogene encoding a serine/threonine-specific protein kinase. Analyses of cDNA and genomic clones of this gene revealed that it was generated by substitution of 5'-sequence (exons 1-5) of the normal c-raf-1 gene with an unrelated human sequence. The region in the genomic clone was identified where the rearrangement had occurred. The rearranged EcoRI fragment was detected in all the primary transformants obtained from two independent transfections, suggesting that the recombination had occurred in the primary cancer. By sequence anal. of cDNA, the putative product of the transforming gene was inferred to have a hydrophobic stretch ahead of the serine/threonine-protein **kinase domain** of the c-**raf-1**
gene product. One of the cDNA which contains the 1.6-kb open reading frame was introduced into the pUC9 vector. An autophosphorylating, 58 kd protein was induced in Escherichia coli cells bearing the plasmid upon induction. Since serine/threonine-protein kinase activity of the normal c-raf protein has not been evidenced, these results suggest that the truncation/replacement of the amino-terminal domain of the c-raf-1 protein leads to constitutive activation of the protein kinase probably residing

on the downstream domain.

L7 ANSWER 34 OF 34 MEDLINE
AB We previously isolated a novel human transforming gene from a primary stomach cancer and identified it as an activated version of the c-raf-1 gene which is the human homologue of v-raf, a viral oncogene encoding a serine/threonine-specific protein kinase. Analyses of cDNA and genomic clones of this gene revealed that it was generated by substitution of 5'-sequence (exons 1-5) of the normal c-raf-1 gene with an unrelated human sequence. We identified the region in the genomic clone where the rearrangement had occurred. The rearranged EcoRI fragment was detected in all the primary transformants obtained from two independent transfections, suggesting that the recombination had occurred in the primary cancer. By sequence analysis of cDNA, the putative product of the transforming gene was inferred to have a hydrophobic stretch ahead of the ser/thr-protein **kinase domain** of the c-**raf-1** gene
product. We introduced one of the cDNA which contains the 1.6-kb open reading frame into the pUC9 vector. An autophosphorylating, 58 kd protein was induced in Escherichia coli cells bearing the plasmid upon induction. Since ser/thr-protein kinase activity of the normal c-raf protein has not been evidenced, these results suggest that the truncation/replacement of the amino-terminal domain of the c-raf-1 protein leads to constitutive activation of the protein kinase probably residing on the downstream domain.

```
=> S (CRAF OR RAF-1)(5a) (mutant or variant)
   9 FILES SEARCHED...
L8         1013 (CRAF OR RAF-1)(5A) (MUTANT OR VARIANT)

=> s l8 and 375
L9            6 L8 AND 375

=> dup rem l9
PROCESSING COMPLETED FOR L9
L10           1 DUP REM L9 (5 DUPLICATES REMOVED)

=> d

L10  ANSWER 1 OF 1     MEDLINE                                DUPLICATE 1
AN   2001015507     MEDLINE
DN   20459105   PubMed ID: 10887184
TI   Point mutants of c-raf-1 RBD with elevated
     binding to v-Ha-Ras.
AU   Fridman M; Maruta H; Gonez J; Walker F; Treutlein H; Zeng J; Burgess A
CS   Ludwig Institute for Cancer Research, P. O. Box 2008, Royal Melbourne
     Hospital, Victoria 3050, Australia.
SO   JOURNAL OF BIOLOGICAL CHEMISTRY, (2000 Sep 29) 275 (39) 30363-71.
     Journal code: 2985121R. ISSN: 0021-9258.
CY   United States
DT   Journal; Article; (JOURNAL ARTICLE)
LA   English
FS   Priority Journals
EM   200010
ED   Entered STN: 20010322
     Last Updated on STN: 20010322
     Entered Medline: 20001027


=> s l8 and lysine
L11           4 L8 AND LYSINE

=> dup rewm l11
ENTER REMOVE, IDENTIFY, ONLY, OR (?):rem
'REWM' IS NOT VALID.  VALID FILE NAMES ARE 'EMBASE, HCAPLUS, BIOTECHNO'
You have entered a file name of duplicates to keep that is not
referenced by any of the L#s specified for this DUPLICATE command.
The file names of duplicates that can be kept are listed above.
Please enter one of these file names.
```

```
=> dup rem l11
PROCESSING COMPLETED FOR L11
L12           3 DUP REM L11 (1 DUPLICATE REMOVED)

=> d 1-3

L12  ANSWER 1 OF 3  HCAPLUS  COPYRIGHT 2003 ACS
AN   2000:808202  HCAPLUS
DN   134:111865
TI   c-Raf-1 RBD Associates with a Subset of Active v-H-Ras
AU   Fridman, Masha; Walker, Francesca; Catimel, Bruno; Domagala, Teresa; Nice,
     Edouard; Burgess, Antony
CS   Ludwig Institute for Cancer Research, Royal Melbourne Hospital, Victoria,
     3050, Australia
SO   Biochemistry (2000), 39(50), 15603-15611
     CODEN: BICHAW; ISSN: 0006-2960
PB   American Chemical Society
DT   Journal
LA   English
RE.CNT  44    THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD
              ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12  ANSWER 2 OF 3  EMBASE  COPYRIGHT 2003 ELSEVIER SCI. B.V.DUPLICATE 1
AN   1999061407  EMBASE
TI   Nuclear magnetic resonance and molecular dynamics studies on the
     interactions of the Ras-binding domain of Raf-1 with
     wild-type and mutant Ras proteins.
AU   Terada T.; Ito Y.; Shirouzu M.; Tateno M.; Hashimoto K.; Kigawa T.;
     Ebisuzaki T.; Takio K.; Shibata T.; Yokoyama S.; Smith B.O.; Laue E.D.;
     Cooper J.A.
CS   S. Yokoyama, Cellular Signaling Laboratory, Institute Physical Chemical
     Research, 2-1 Hirosawa, Wako-shi, Saitama 351-0198, Japan.
     yokoyama@y-sun.biochem.s.u.-tokyo.ac.jp
SO   Journal of Molecular Biology, (12 Feb 1999) 286/1 (219-232).
     Refs: 74
     ISSN: 0022-2836  CODEN: JMOBAK
CY   United Kingdom
DT   Journal; Article
FS   029     Clinical Biochemistry
LA   English
SL   English

L12  ANSWER 3 OF 3  HCAPLUS  COPYRIGHT 2003 ACS
AN   1998:557895  HCAPLUS
DN   129:256913
TI   Identification of residues in the cysteine-rich domain of Raf-1 that
     control Ras binding and Raf-1 activity
AU   Winkler, David G.; Cutler, Richard E., Jr.; Drugan, Jonelle K.; Campbell,
     Sharon; Morrison, Deborah K.; Cooper, Jonathan A.
CS   Fred Hutchinson Cancer Research Center, Seattle, WA, 98109-1024, USA
SO   Journal of Biological Chemistry (1998), 273(34), 21578-21584
     CODEN: JBCHA3; ISSN: 0021-9258
PB   American Society for Biochemistry and Molecular Biology
DT   Journal
LA   English
RE.CNT  48    THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD
              ALL CITATIONS AVAILABLE IN THE RE FORMAT


=> d 1, 3 ab

L12  ANSWER 1 OF 3  HCAPLUS  COPYRIGHT 2003 ACS
AB   Mutational anal. of the cRaf-1 Ras binding domain (RBD) identified several
     point mutants with elevated Ras binding.  Detailed examn. of the binding
     kinetics of one mutant (A85K) suggests that it assocs. with a greater
     range of isomeric conformers of v-H-Ras than wt.-RBD.  At limiting v-H-Ras
     concns., satn. binding to A85K-RBD is higher than to wt.-RBD.  Notably, in
     assay systems where the RBD concn. is limiting, no difference exists
```

between wt.-RBD and A85K-RBD satn. levels in the presence of sufficiently large molar excess of Ras. The inability of wt.-RBD to sat. all bindable Ras/GTP (defined by its binding to A85K-RBD) suggests that Ras/GTP exists as several isoforms and that only a minority of these isoforms are capable of assocg. with wt.-RBD. These findings provide the first exptl. evidence in support of functionally distinct Ras/GTP isoforms. We also describe a novel anal. of such isoforms.

L12 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2003 ACS
AB We have identified mutations in Raf-1 that increase binding to Ras. The mutations were identified making use of three mutant forms of Ras that have reduced Raf-1 binding (Winkler, D. G., Johnson, J. C., Cooper, J. A., and Vojtek, A. B. (1997) J. Biol. Chem. 272, 24402-24409). One mutation in **Raf-1**, N64L, suppresses the Ras **mutant** R41Q but not other Ras mutants, suggesting that this mutation structurally complements the Ras R41Q mutation. Missense substitutions of residues 143 and 144 in the Raf-1 cysteine-rich domain were isolated multiple times. These **Raf-1 mutants**, R143Q, R143W, and K144E, were general suppressors of three different Ras mutants and had increased interaction with non-mutant Ras. Each was slightly activated relative to wild-type Raf-1 in a transformation assay. In addn., two mutants, R143W and K144E, were active when tested for induction of germinal vesicle breakdown in Xenopus oocytes. Interestingly, all three cysteine-rich domain mutations reduced the ability of the Raf-1 N-terminal regulatory region to inhibit Xenopus oocyte germinal vesicle breakdown induced by the C-terminal catalytic region of Raf-1. We propose that a direct or indirect regulatory interaction between the N- and C-terminal regions of Raf-1 is reduced by the R143W, R143Q, and K144E mutations, thereby increasing access to the Ras-binding regions of Raf-1 and increasing Raf-1 activity.

=> d l7 4, 6, 14, 20, 23, 26, 33

L7 ANSWER 4 OF 34 MEDLINE DUPLICATE 3
AN 2001223718 MEDLINE
DN 21061396 PubMed ID: 10998357
TI Regulation of the **Raf-1 kinase domain** by phosphorylation and 14-3-3 association.
AU Yip-Schneider M T; Miao W; Lin A; Barnard D S; Tzivion G; Marshall M S
CS Department of Medicine, Indiana University School of Medicine, Indianapolis, IN 46202, USA.
SO BIOCHEMICAL JOURNAL, (2000 Oct 1) 351 (Pt 1) 151-9.
Journal code: 2984726R. ISSN: 0264-6021.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200104
ED Entered STN: 20010502
Last Updated on STN: 20010502
Entered Medline: 20010426

L7 ANSWER 6 OF 34 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT AND ISI
AN 1999-05589 BIOTECHDS
TI New isolated human nucleic acid unique to c-raf-1; human c-raf-1 having point mutation in conserved region, may be useful for lung adenocarcinoma susceptibility diagnosis
AU Rapp U R; Storm S M
PA U.S.Dep.Health-Hum.Serv.
LO Washington, DC, USA.
PI US 5869308 9 Feb 1999
AI US 1997-831317 1 Apr 1997
PRAI US 1997-831317 1 Apr 1997
DT Patent
LA English
OS WPI: 1999-152776 [13]

L7 ANSWER 14 OF 34 MEDLINE DUPLICATE 12

AN 97429918 MEDLINE
DN 97429918 PubMed ID: 9285556
TI Mutations of critical amino acids affect the biological and biochemical properties of oncogenic A-Raf and Raf-1.
AU Bosch E; Cherwinski H; Peterson D; McMahon M
CS Department of Cell Signaling, DNAX Research Institute, Palo Alto, California 94304-1104, USA.
SO ONCOGENE, (1997 Aug 28) 15 (9) 1021-33.
Journal code: 8711562. ISSN: 0950-9232.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199709
ED Entered STN: 19971008
Last Updated on STN: 20000303
Entered Medline: 19970922

L7 ANSWER 20 OF 34 MEDLINE DUPLICATE 18
AN 95294017 MEDLINE
DN 95294017 PubMed ID: 7539798
TI Functional mapping of the N-terminal regulatory domain in the human Raf-1 protein kinase.
AU Chow Y H; Pumiglia K; Jun T H; Dent P; Sturgill T W; Jove R
CS Department of Microbiology and Immunology, University of Michigan Medical School, Ann Arbor 48109, USA.
NC CA55652 (NCI)
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1995 Jun 9) 270 (23) 14100-6.
Journal code: 2985121R. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199507
ED Entered STN: 19950720
Last Updated on STN: 20000303
Entered Medline: 19950710

L7 ANSWER 23 OF 34 MEDLINE DUPLICATE 21
AN 95408256 MEDLINE
DN 95408256 PubMed ID: 7545901
TI The 33-kDa C-terminal domain of Raf-1 protein kinase exhibits a Ras-independent serum- and phorbol ester-induced shift in gel mobility.
AU Olah Z; Ferrier A; Lehel C; Anderson W B
CS Laboratory of Cellular Oncology, National Cancer Institute, National Institutes of Health, Bethesda, MD 20892, USA.
SO BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (1995 Sep 14) 214 (2) 340-7.
Journal code: 0372516. ISSN: 0006-291X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199510
ED Entered STN: 19951026
Last Updated on STN: 20000303
Entered Medline: 19951019

L7 ANSWER 26 OF 34 HCAPLUS COPYRIGHT 2003 ACS
AN 1993:492494 HCAPLUS
DN 119:92494
TI Oncogene activation: c-raf-1 gene mutations in experimental and naturally occurring tumors
AU Storm, Stephen M.; Rapp, Ulf R.
CS Frederick Cancer Res. Dev. Cent., Frederick, MD, USA
SO Toxicology Letters (1993), 67(1-3), 201-10
CODEN: TOLED5; ISSN: 0378-4274
DT Journal; General Review
LA English

L7 ANSWER 33 OF 34 HCAPLUS COPYRIGHT 2003 ACS
AN 1988:487252 HCAPLUS
DN 109:87252
TI Structure of the activated c-raf-1 gene from human stomach cancer
AU Shimizu, Kenji; Nakatsu, Yoshimichi; Nomoto, Satoshi; Sekiguchi, Mutsuo
CS Fac. Sci., Kyushu Univ., Fukuoka, 812, Japan
SO Proceedings of the International Symposium of the Princess Takamatsu Cancer Research Fund (1987), Volume Date 1986, 17th(Oncog. Cancer), 85-91
CODEN: PPTCBY
DT Journal
LA English

=> DIS HIS

(FILE 'HOME' ENTERED AT 19:42:11 ON 08 JUL 2003)

FILE 'MEDLINE, SCISEARCH, LIFESCI, BIOTECHDS, BIOSIS, EMBASE, HCAPLUS, NTIS, ESBIOBASE, BIOTECHNO, WPIDS' ENTERED AT 19:42:28 ON 08 JUL 2003

L1 175856 S ZHOU, ?/AU
L2 13860 S L1 AND PY=1998
L3 8 S L2 AND RAF-ERK
L4 1 DUP REM L3 (7 DUPLICATES REMOVED)
L5 1 S (CRAF OR RAF-1) AND (1-305 OR 306-648)
L6 175 S (CRAF OR RAF-1)(5A) KINASE DOMAIN
L7 34 DUP REM L6 (141 DUPLICATES REMOVED)
L8 1013 S (CRAF OR RAF-1)(5A) (MUTANT OR VARIANT)
L9 6 S L8 AND 375
L10 1 DUP REM L9 (5 DUPLICATES REMOVED)
L11 4 S L8 AND LYSINE
L12 3 DUP REM L11 (1 DUPLICATE REMOVED)

=> LOG H

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